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EDITORIAL

THE ANAESTHETIST AND NERVE BLOCKING

VISITORS to hospitals in the United States are often confused at first by the use of the words "Anesthesiologist" (a specialist in the science of anaesthesia) and "Anesthetist" (one who administers anaesthetics). The former is a qualified medical practitioner while the latter is either a trained nurse or technician. In this country, where all anaesthetics are administered by medical practitioners—with the exception of the few given by medical students under direct supervision—this division of anaesthetists into "specialists" and "technicians" does not exist. Nevertheless, by virtue of the requirements of modern anaesthesia together with the sessional system and amount of work to be done, the anaesthetist must of necessity spend the majority of his time in the operating theatre, and there is always the danger of a qualified practitioner gradually becoming simply a technician whose sole duty is to provide first-rate operating conditions for an endless variety of surgical procedures.

During his long training period five or six years at least are spent at medical school, a minimum of one year is occupied by the routine work as a house surgeon and house physician and usually a further five to seven years in various anaesthetic trainee posts before he can reasonably hope to obtain consultant status. The examination for the Fellowship of the Faculty of Anaesthetists of the Royal College of Surgeons not only requires a detailed knowledge of the action of anaesthetic drugs and of various techniques, but also a detailed study of anatomy, physiology, pharmacology and pathology. The extent of this latter knowledge is well outside the minimum requirements necessary for simply administering anaesthetics. It qualifies the anaesthetist to help in the pre-operative preparation and postoperative care of surgical cases and to be an integral part of the surgical team.

In recent years the activities of the anaesthetist have more and more extended outside the operating theatre. Their help is frequently requested in the management of respiratory paralysis and in cases of tetanus. In this issue Dr. J. R. J. Beddard records his long experience in the field of nerve blocking both for surgical anaesthesia and as a diagnostic, prognostic or therapeutic measure. Despite numerous advances in general anaesthesia in recent years, there are still many instances where local anaesthesia is the technique of choice. Failure of anaesthetists to practise such blocks when the occasion arises in fit subjects, may be regretted when their success is a matter of great importance.

In the management of intractable pain from malignant disease with nerve blocks, the anaesthetist will find his most rewarding results. In this field he can best achieve the requirements suggested by Sir Francis Bacon: ". . . not only to restore health but to mitigate pain and dolors". The management of such cases has been a problem since time immemorial and in 1852 Jacob Bigelow (who incidentally wrote the famous letter from Boston in 1846 to Francis Boott in London describing Morton's first demonstration of the anaesthetic properties of ethyl ether) wrote:

> When we know that a case is self-limited or incurable, we are to consider how far it is in our power to palliate or diminish sufferings which we are not competent to remove. Here is a most important field for medical practice and one which calls for an exceedingly large portion of the time and efforts of every physician. When we consider that most diseases occupy, from necessity, a period of some days or weeks, that many of them continue for months and some for years, and finally that a large portion of mankind die of some lingering or chronic disease, we shall see that the study of palliatives is not only called for, but really constitutes one of the most common, as well as the most useful and beneficent employments of a medical man.

At present we are handicapped by the lack of an innocuous reliable drug for the production of permanent anaesthesia. Beddard has found like many others, that results with Proctocain and Efocain are disappointing. Absolute alcohol is limited to intrathecal injections and to nerve trunks or ganglia where anatomical accuracy of injection is possible. It is to be hoped that Maher's phenol-glycerine (or phenol-myodil) solution may prove the solution of choice in such cases and preliminary reports by Nathan and Scott (1958) seem promising. Perhaps not enough use is made of oily cinchocaine (Nupercaine) which contains 10 per cent benzyl alcohol, since the prolonged action of the oily solutions is, in fact, due to the degeneration caused by benzyl alcohol on the nerves (Duncan and Jarvis, 1943).

The most complete guide to therapeutic nerve blocks is without doubt that of Bonica (1953). The title of this 1,533-page volume, *The Management of Pain*, is worthy of consideration. Anaesthetists should not be content simply to carry out nerve blocks at the request of their surgical or medical colleagues. Even in this field they can find themselves relegated to technician "anesthetists". The specialist "anesthesiologist", with his detailed knowledge of the pharmacology of the analgesic drugs and their adjuvants has more to offer in the management of intractable pain than the ability to place solutions near the required nerves. Too many patients who are past the help of therapeutic nerve blocks find themselves, like Friedrich Sertürner (the discoverer of morphine), also in a state where even the opiates will no longer give relief. Part of this dilemma is undoubtedly due to the too early and too generous use of these drugs, without recourse to the numerous available synthetic analgesics and adjuvants. Here the services of the well informed anaesthetist are most welcomed by his colleagues.

Bonica (1958) has admirably outlined the role of the anaesthetist in this field as follows: "He can contribute significantly to the solution of many difficult diagnostic and therapeutic problems, but he must assume responsibility and discharge his obligations as a physician rather than act as a technician, expert in inserting needles."

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RESERPINE AND VASCULAR TONE*

BY

J. H. BURN

The Department of Pharmacology, University of Oxford

THE DISTRIBUTION OF NORADRENALINE

The task which I have set before me in preparing this lecture is an ambitious one, for it is no less than to suggest that there is a factor playing a part in the control of vascular tone which has hitherto been neglected. The view I shall put forward is based on work which has been done jointly with my colleague Dr. Michael J. Rand (Burn and Rand, 1958, a, b). I may begin by pointing out that in 1946 an important discovery was made, when v. Euler described the presence in sympathetic nerves of a chemical substance related in structure to adrenaline, but differing from it in not having a $-CH_3$ group attached to the nitrogen atom, so that it was called noradrenaline. v. Euler suggested that this was the humoral transmitter of the impulses passing down the sympathetic nerves, the impulse becoming effective by the liberation of some noradrenaline.

However, in 1948, Schmiterlöw first showed that noradrenaline had a wider distribution. He found that noradrenaline was present in the walls of arteries and veins also, being particularly abundant in the outer part of the wall where the nerves entered. In 1951 v. Euler and Purkhold estimated the amounts present in other organs, such as the spleen, the kidney, the liver and the salivary glands of the sheep, and in the same year Goodall estimated the amount in the heart. Noradrenaline was present in all these organs. Both v. Euler and Purkhold on the one hand and Goodall on the other studied the effect of removing the sympathetic fibres, and they observed that after a week or two the amount of noradrenaline in the organs was very much less.

However, from that time until now there has been no indication of the function of noradrenaline present in these organs, and most workers appear to have regarded it as an inert store.

ACTION OF NICOTINE ON THE HEART

Our own approach to this problem has been largely accidental, depending chiefly on our interest in the action of nicotine. We are pharmacologists studying the effect of drugs, and it is proper that we should always be interested in a substance which is probably the most widely used drug of all. I will describe first some observations on the heart.

We have made many studies in the Oxford laboratory, not on the heart itself, but on the auricles or atria, which are easily dissected from the heart when this is removed from a rabbit. They can be suspended in a bath so that their contractions are recorded by a lever writing on a drum. In 1953 I asked my colleague Kottegoda to study the action of nicotine in this preparation. Now nicotine is known to be a substance which stimulates ganglia, so that the ganglion cells send impulses along their fibres. In the rabbit atria there are ganglion cells around which the fibres of the vagus nerves terminate, and the ganglion cells transmit the vagal impulses to the atrial tissue. We therefore expected that when nicotine was added to the bath in which the atria were suspended, the contractions would become slower or they would stop altogether. Adding nicotine would be like stimulating the vagus.

Actually, however, little inhibitory effect was seen, and we were surprised to find that it was overcome by a stimulant effect which became more evident when the nicotine had been in the bath for 1–2 minutes. By adding some atropine, and thus excluding inhibition, the stimulant phase of the nicotine action was seen quite clearly. There was no possibility in 1953 of analyzing this stimulant action further. It was obviously an

* Lecture delivered at the Charing Cross Hospital Medical School on April 30, 1958.

action like that of adrenaline, and since we knew from Goodall's work that some noradrenaline and adrenaline were present in the heart, we supposed that perhaps nicotine released these substances from whatever structures in which they were held. However, we could not test this idea.

THE ACTION OF RESERPINE

Much interest has been taken in the last five years in an alkaloid reserpine which was isolated from *Rauwolfia*. It has a tranquillizing action in man, and in addition a hypotensive action. It is used chiefly in mental hospitals, but it has to be used with care because it may produce not only tranquillity but also depression, and even melancholy. When it was found to deplete certain regions of the brain of hydroxytryptamine, its tranquillizing action was ascribed to the loss of this substance. However, in 1956, it was found to deplete the adrenal glands of adrenaline and noradrenaline, and later it was shown to deplete the brain of these substances also, so that its tranquillizing action might as well be explained by this action.

In the same year, 1956, Bertler, Carlsson and Rosengren made the observation that when reserpine was given to rabbits it caused the noradrenaline and the adrenaline present in the heart to disappear. Whereas the hearts of normal rabbits contained a mean amount of 1.57 μg/g reckoned as noradrenaline, the hearts from rabbits treated with reserpine and killed 16 hours later contained only 0.03 μg/g. We therefore examined the atria from rabbits injected with reserpine, and found that the stimulant action of nicotine was completely absent. This observation confirmed the view that the stimulant action was due to the liberation of noradrenaline and adrenaline from the stores in the heart.

NORMAL ACTION OF THE NORADRENALINE STORE

In the course of our observations we found that the rate at which the atria contracted when suspended in the isolated organ bath at 30°C differed according to their origin. Atria from normal rabbits contracted more quickly, the mean rate for nine atria being 146 per minute, while atria from rabbits treated with reserpine contracted more slowly, the mean rate for eleven atria being 112 per minute. This difference was highly significant ($P<0.001$) and it demonstrated that the store of noradrenaline is not an inactive store, but that it slowly releases noradrenaline, which affects the rate of the pacemaker.

ACTION OF NICOTINE ON BLOOD VESSELS

Beginning in 1913 with an observation made by Handovsky and Pick, a series of workers, of whom Loewi was one, observed that nicotine had a direct constrictor action on blood vessels. The common teaching concerning nicotine is that it causes vasoconstriction by its action on sympathetic ganglia, and the evidence that it has in addition an action on the vessels themselves is not widely known. In 1953, at my suggestion, Kottegoda studied this action in the perfused vessels of the rabbit ear, and observed first that it was abolished by hexamethonium, just as the action of nicotine on sympathetic ganglia is abolished with hexamethonium. Then he made a second observation. It has long been known that the constrictor action of adrenaline is reversed to a dilator action by certain substances of which the first was ergotoxine (Dale, 1906). A substance introduced more recently which reverses the action of adrenaline is tolazoline (Priscol) and Kottegoda found that when this substance was added to the solution perfusing the vessels of the rabbit ear, not only was the action of adrenaline and of noradrenaline reversed, but the action of nicotine was reversed also. Thus his evidence suggested that in the vessels, as well as in the heart, nicotine released noradrenaline, and perhaps also a smaller amount of adrenaline, from the store in the vessel wall, and that the vasoconstriction caused by nicotine was due to the noradrenaline so released. Kottegoda made a third observation. He found that when the skin was removed from the rabbit's ear, there was still a network of vessels lying on the cartilage underneath. On these vessels nicotine had no constrictor action.

EFFECT OF RESERPINE ON THE VESSELS

In view of the results on the atria of rabbits treated with reserpine, we therefore studied the action of nicotine on the perfused ears of rabbits treated with reserpine. We found that in these ears nicotine had no constrictor action. We therefore extracted the skin of rabbit ears to see if we could detect the presence of noradrenaline, and we found that in extracts of the skin of normal

rabbits there was a substance behaving like noradrenaline. We detected its presence by injecting the extract intravenously into rats and observing the rise of blood pressure. However, in the skin of the ears of rabbits injected with reserpine no such substance was present, for the extracts had no pressor activity. The mean amount present in the skin of normal rabbit ears was 0.1 μg/g.

Now Adams-Ray and Nordenstam (1956) have found chromaffin cells in human skin, which are cells containing adrenaline in granules which take certain stains. We therefore wondered if chromaffin cells were present in the skin of rabbit ears. Mr. E. H. Leach, of the University Department of Physiology, very kindly examined the ears of two normal rabbits and of two rabbits treated with reserpine. He found chromaffin cells in the normal rabbit ears adjoining the blood vessels; but they were absent from the ears of rabbits treated with reserpine. It therefore seemed possible that the constrictor action of nicotine in normal ears was due to nicotine releasing adrenaline from chromaffin cells.

We remembered, however, that Schmiterlöw (1948) had observed the presence of noradrenaline in artery walls, and we therefore extracted the aortae of a series of rabbits, some normal and some treated with reserpine. We found by testing the extracts on the rat blood pressure that the normal aortae contained a mean amount of 0.5 μg/g of material estimated as noradrenaline, while the aortae from reserpine-treated rabbits contained less than one-fifth of this.

ACTION OF NICOTINE ON THE VASCULAR SYSTEM

We have known for a long time that smoking accelerated the heart rate and that it caused peripheral vasoconstriction, but we have supposed that this was an effect of nicotine on sympathetic ganglia. We now see that it is probably also an effect of nicotine on the store of noradrenaline and adrenaline in the heart and in or near the blood vessels. This makes it easier to understand the drop in skin temperature which Roth, McDonald and Sheard (1944) have recorded during smoking, and the great fall in blood flow through the hand.

There appears to be general agreement that the relation of smoking to thromboangiitis obliterans is well established. Wright (1955) states that the disease will rarely become or remain quiescent, and that gangrene and ulcers will continue indolent or progress adversely, so long as the patient continues to smoke even occasionally. Furthermore, even after the lesions have healed and the disease has remained quiescent for months, or even years, while the patient has not smoked, the renewal of the use of tobacco will almost invariably be followed within a few weeks or months by reactivation of the disease. This situation can be understood more easily if nicotine causes excessive vasoconstriction by releasing adrenaline or noradrenaline either from the artery wall or from chromaffin cells adjoining it.

OTHER SUBSTANCES RELEASING NORADRENALINE

If I may be forgiven for saying something on what may seem a purely academic pharmacological topic, I will add that we have found other substances besides nicotine which release noradrenaline from the store in the artery walls. Carlsson and his colleagues (1957) observed that in cats treated with reserpine, the amine tyramine did not cause a rise of blood pressure. Tyramine is almost the simplest substance possessing the skeleton of adrenaline, and from the time it was first examined by Dale and Dixon (1909) it has been thought of as a substance acting like adrenaline but in a feebler fashion. Carlsson and his colleagues did not discuss their observation except that they said it is known that for the normal action of tyramine the adrenergic nervous system must be intact.

Since we had discovered that in the reserpine-treated cat the store of noradrenaline disappeared from the artery walls, we were at once led to suppose that the tyramine failed to cause its rise of blood pressure, because its normal method of causing a rise was by releasing noradrenaline from the store, and that tyramine was a substance which might be called an adrenaline liberator rather than a substance which acted like adrenaline.

Other differences between adrenaline and tyramine were recorded many years ago. Fröhlich and Loewi (1910) showed that cocaine increased the action of adrenaline, but Tainter and Chang (1927) showed that cocaine abolished the action of tyramine. Again when tissues were denervated by cutting the sympathetic supply, the effect of

adrenaline was increased, but the effect of tyramine and of ephedrine was abolished (Burn and Tainter, 1931; Burn, 1932). Hence previous work supplied some justification for the view that the difference between adrenaline and tyramine was not merely a quantitative difference, but that it was a difference in kind.

In confirmation of Carlsson and his colleagues we observed that in the spinal preparation of a cat previously given reserpine, tyramine had only a slight pressor action and that it did not cause contraction of the nictitating membrane. At the same time the pressor action of noradrenaline was much greater than normal, as was shown by Bein, Gross, Meier and Tripod (1953). Evidence in favour of the view that the pressor action of tyramine was due to the lack of noradrenaline in the artery wall was that when an infusion of 1 mg noradrenaline was given during a period of about 15 minutes, and when the effect of this infusion on the blood pressure had subsided, the injection of tyramine was followed by a much greater pressor effect. It appeared as if the noradrenaline circulating in the blood had partly refilled the store in the artery wall. It was of interest to me that I had made the same observation in 1932 in experiments on the perfused hind leg of the dog. I then found that, in the perfused leg, tyramine had much less constrictor action compared with adrenaline than was to be expected from its pressor action in the spinal cat, but that when adrenaline was slowly infused into the blood, the constrictor action of tyramine increased. Not only was the effect of tyramine increased, but the effect of sympathetic stimulation was also increased, and this too we have recently confirmed.

Our results have then led us to the view that the sympathomimetic amines can be divided into two classes: those which act directly on the vessels, and those which liberate adrenaline, or more probably noradrenaline, from the vessel walls. The vessels of reserpine-treated animals are highly sensitive to the substances which act directly, which include noradrenaline, adrenaline and dopamine, and they exert a given pressor effect in much smaller doses than in normal animals. The vessels and the nictitating membranes of reserpine-treated animals are, however, insensitive to the action of substances like tyramine, phenylethylamine, amphetamine, ephedrine and the D form of phenylethanolamine. Their action in the reserpine-treated animal is restored by an intravenous infusion of noradrenaline, but not, I may point out, by an intravenous infusion of hydroxytryptamine. We therefore think that these substances exert their normal action on the vessels and the nictitating membrane by liberating noradrenaline.

INTRAVENOUS DRIP OF NORADRENALINE

Returning now to more practical considerations which are of interest to others than pharmacologists, I think that our results throw light on a phenomenon which has puzzled surgeons and particularly anaesthetists. Since the introduction of noradrenaline, the practice has increased of using an intravenous drip to maintain the blood pressure in circumstances in which it has fallen low. This is not an easy method of maintaining the blood pressure because fluctuations in the speed of the drip cause large variations in the blood pressure. The chief disadvantage, however, is that when the drip is finally stopped, the blood pressure very often falls abruptly, and the patient's condition is only restored when the drip is started again. There are a good many cases on record of the drip having to be continued for two or three days, and I have heard of it being continued for much longer periods. The fall of blood pressure on stopping the drip has also been observed in rabbits by Blacket, Pickering and Wilson (1950).

The problem is to know what has happened to the normal sympathetic tone, which seems to be strangely deficient as a result of the continued infusion of noradrenaline. One cause of the deficiency may be ganglionic block, for in 1939 Marazzi observed that adrenaline depressed the transmission of impulses through a sympathetic ganglion, and his observations were confirmed by Bülbring and Burn in 1941. A second cause which seems perhaps more important is the effect of the noradrenaline infusion on the response of the vessel wall to sympathetic impulses. We have seen that in the cat or dog treated with reserpine, not only is the pressor effect of tyramine very feeble, but the pressor effect of noradrenaline is unusually great. These changes appear to depend on the disappearance of the store of noradrenaline in the vessel wall. When, however, an intravenous

infusion of noradrenaline is given during a period of 15 or 20 minutes, which results in a building up of the store in the vessel wall at the end of this time, then when the effect of the intravenous infusion on the blood pressure has passed off, the pressor effect of noradrenaline is very small. The same diminution in sensitivity to noradrenaline occurs in a normal animal when an intravenous infusion of noradrenaline is given. From these observations it appears to follow that the sensitivity of the vessel wall to the action of noradrenaline depends on the size of the store of noradrenaline present in the wall. Now since the sympathetic nerves act by liberating noradrenaline we may say that the sensitivity of the vessel wall to sympathetic impulses depends on the size of the store of noradrenaline present in the wall. Thus when the store is large, as after the intravenous infusion of noradrenaline, the sensitivity of the vessel wall to sympathetic impulses is very low, and it is for this reason that the abrupt fall of blood pressure occurs when the intravenous drip of noradrenaline is stopped.

This account may perhaps seem like special pleading which may have some relation to the true state of affairs or not. But it is more than that, for a practical suggestion emerges from it. The suggestion is that when the blood pressure of a patient has been maintained for some time by an intravenous drip of noradrenaline, and when there has been an alarming fall of blood pressure on stopping the drip, the correct procedure then is not to restart the drip, but to give an injection of ephedrine which causes a discharge of noradrenaline from the store in the vessel walls. Ephedrine as we have seen acts like tyramine and phenylethylamine as an adrenaline liberator, and its effect is greatest when the store in the vessel walls is greatest. But ephedrine is more suited for injection in these circumstances than tyramine or phenylethylamine for these two substances are soon destroyed by amine oxidase. Ephedrine, however, having a methyl group on the α-carbon atom, cannot be destroyed by amine oxidase, and therefore goes on acting for a much longer time. It is, of course, always risky to assume that what happens in the cat or the dog will also happen in man, but the assumption in this case seems to me justifiable.

PERIPHERAL VASCULAR DISEASES

I may now turn to a different subject, that of peripheral vascular disease, for it will be clear that the store of noradrenaline in the vessel wall may be a contributory or even a causal factor here. We have found that there is a steady leak from the store in the heart, since the rate of isolated atria is much slower when the store is no longer there, and it is therefore likely that there is a leak from the store in the vessels. Hitherto no one has determined what happens to the store in the vessels when the nerve supply degenerates, but v. Euler and Purkhold made observations in the spleen, the liver, the kidneys and the salivary glands, and in all these tissues the store of noradrenaline declined to a small fraction of its original value.

We can readily suppose that the cold blue fingers of those with Raynaud's disease, and the symptoms of Buerger's disease, are due to a leak of noradrenaline from the store in the artery wall which is greater than the leak in ordinary individuals. If this is so, some relief of the symptoms should be obtained by the use of reserpine which will disperse the store in the walls. Scalfi, Jacono and Juliani (1956) have indeed given reserpine to thirteen cases of arterial disease, recording vasodilatation in the fingers by photoplethysmography. They found that when 1 mg reserpine was injected intramuscularly there was prolonged vasodilatation in eight of the cases. Three were cases of Raynaud's disease and dilatation occurred in two; in the other case of this disease lesions of scleroderma were present. These authors did not explain why they had tried reserpine, and they did not use reserpine for treatment.

Patients with Raynaud's disease are usually benefited by sympathectomy for a period of several months, but often at the end of a year they are no longer improved. The early benefit from sympathectomy is probably due to a fall in the store of noradrenaline in the artery wall, though this has not yet been directly observed. It may, however, be inferred, provisionally at least, since, as already described, a fall has been shown to occur in other organs, like the spleen, after sympathetic denervation. The later deterioration and return of the symptoms may perhaps be explained by the vessels picking up noradrenaline from the amount circulating in the blood, secreted

into the blood from the adrenal glands. Thus the store may be replenished although the vessel is denervated.

From these considerations it is clear that reserpine may prove a satisfactory treatment for peripheral vascular disease in some patients at least. But reserpine has central effects producing depression. The usefulness of reserpine for any given patient will probably depend on whether the peripheral effect on the vessels can be obtained without producing central effects which are too severe.

RESERPINE IN THE TREATMENT OF HYPERTENSION

Apart from peripheral vascular disease there is the question of its action in hypertension, and here I will refer to the interesting observation made by Harington (1956) that some three or four hours after an intravenous injection of 3 mg reserpine the effect of an injection of hexamethonium was greatly increased. He observed this in six patients.

The effect of reserpine on vascular tone is not simple. As Bein (1955) has shown, it diminishes the stream of impulses from the sympathetic centres. In addition it removes the store of noradrenaline from the artery walls and in doing so makes them more responsive to such impulses as still arrive. Thus the fall of blood pressure due to the diminution in the central outflow is less than it would be. In other words, under the influence of reserpine the blood pressure falls, but not greatly, because the fewer impulses act on a more sensitive vascular bed containing less noradrenaline. The blood pressure may, however, be more dependent on sympathetic impulses and less on the noradrenaline leaking from the store in the artery wall. When hexamethonium is given, the fall of blood pressure is greater because of the removal of the central impulses which after giving reserpine are the only controlling factor.

In conclusion it may be said that reserpine is proving a most valuable tool for analyzing the factors which control vascular tone. We have learnt that the store of noradrenaline and adrenaline which is present in the heart and in the blood vessels is not inert, but that certain substances such as nicotine and many of the sympathomimetic amines release noradrenaline from it, and indeed that in the heart there is normally a release not due to any known agent. We have learnt that the store controls the sensitivity of the organ to noradrenaline reaching it via the sympathetic nerves or via the blood stream. We have learnt that the store can be replenished from the blood stream. Finally we have some pointers to the better treatment of peripheral vascular disease and perhaps of hypertension itself.

Our own connexion with these developments has come from what might be called idle interest in an obscure and apparently academic pharmacological problem. Sometimes such an interest seems to justify itself.

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VASCULAR RESPONSES TO CARBON DIOXIDE DURING ANAESTHESIA IN MAN

BY

L. McARDLE

The Mater Infirmorum Hospital, Belfast, Northern Ireland

AND

I. C. RODDIE

The Department of Physiology, The Queen's University of Belfast, Northern Ireland

INHALATION of 30 per cent carbon dioxide for 1 to 2 minutes causes a striking increase in resistance to blood flow in the extremities, mainly in the skeletal muscles and largely mediated through vasomotor nerves (McArdle, Roddie, Shepherd and Whelan, 1957). This is accompanied by a marked rise in systolic, diastolic and pulse arterial pressure. In the present paper the effect of general anaesthesia on these responses is described.

METHODS

Observations were made on young women who required minor gynaecological operations under general anaesthesia. Each patient had papaveretum 20 mg and scopolamine 0.4 mg given intramuscularly 1 hour before operation. Anaesthesia was induced by intravenous thiopentone and maintained by nitrous oxide, oxygen and ether using a semiclosed circuit. Immediately after the operation had been completed the first series of observations on the responses of the vascular system to inhalation of 30 per cent carbon dioxide was made, the patient at this time being deeply anaesthetized. Breathing 30 per cent carbon dioxide caused hyperpnoea and this, by facilitating the elimination of the volatile anaesthetics from the body, led to a rapid return of consciousness. When the patient was conscious the observations were repeated.

Forearm blood flow was measured by venous occlusion plethysmography and arterial blood pressure from a needle in the brachial or femoral artery by a capacitance manometer. Respiratory movements were recorded by two stethographs, one round the abdomen and one round the chest connected to a single volume recorder (Shepherd, 1951; Dornhorst and Leathart, 1952). In some experiments the pH of brachial arterial blood was measured using a Cambridge pH meter.

RESULTS

Figure 1 shows the effects of inhaling 30 per cent carbon dioxide in oxygen on arterial blood pres-

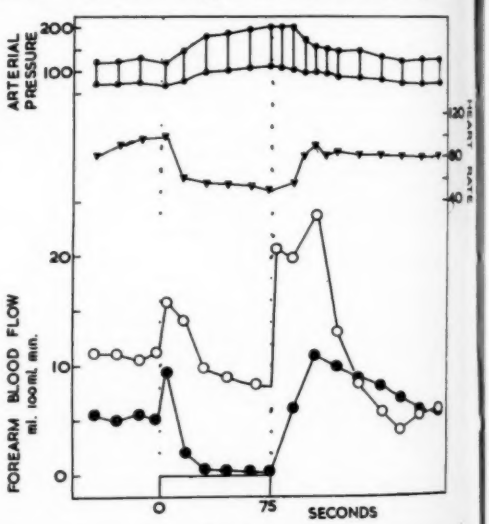

FIG. 1

The effect of inhaling 30 per cent carbon dioxide on arterial blood pressure, heart rate and forearm blood flow in the conscious subject.

● Normal forearm. ○ Nerve blocked forearm.

sure, heart rate and forearm blood flow in the conscious subject. The arterial pressure rose from about 120/75 to about 210/100 mm Hg. This was associated with slowing of the heart rate. The forearm blood flow, after an initial transient increase was greatly reduced during the inhalation. In the nerve-blocked forearm a similar fall did not occur, indicating that vasomotor nerves were largely responsible for the fall in flow in the normal forearm. The fall in flow in the normal forearm in spite of the large increase in arterial pressure indicated that the blood vessels in these parts were intensely constricted. When the inhalation stopped there was a transient vasodilatation before the flows returned to their resting level.

General anaesthesia greatly modified these responses. Figure 2 shows arterial pressure records from one patient comparing the pressure responses to carbon dioxide during and after anaesthesia. When the patient was conscious the usual pressor response was seen, but when anaesthetized the arterial pressure was only very slightly increased. When conscious, the heart rate slowed, whereas when anaesthetized it increased slightly. The changes in blood flow in the periphery were also modified by anaesthesia (fig. 3, table I). Though the flows decreased in the usual manner in the conscious patient when carbon dioxide was breathed there was either little change or an increase in flow when the patient was anaesthetized. The transient vasodilatation which occurred when the inhalation stopped was not noticeably affected by anaesthesia. However, the transient vasodilatation which occurred immediately after the inhalation began was not seen when the patient was anaesthetized.

The respiratory response to carbon dioxide was also depressed by general anaesthesia. It was therefore thought possible that the depression of the respiratory response might result in less carbon dioxide being taken up by the lungs than in the conscious patient with normal respiratory reflexes and that this difference might account for the differences in the vascular responses. It was found, however, that the fall in arterial blood pH with 30 per cent carbon dioxide inhalation was similar in the conscious and the anaesthetized patient (fig. 4). It seemed more likely, therefore, that the differences in the responses were due to a general depression of reflex activity resulting from the anaesthesia. This conclusion was supported by the results of the following experiments. Forearm blood flow was measured in four patients (fig. 5). When the legs were passively raised, forearm blood flow increased. This was due to reflex vasodilatation in skeletal muscle (Roddie and Shepherd, 1956, 1958). When the patient was anaesthetized the increase in forearm blood flow with leg raising was either considerably reduced or absent.

Figures 6 and 7 show the results of two experiments on two patients where resistance to flow in the forearm was calculated by dividing mean perfusion pressure by mean blood flow during and after anaesthesia. In both cases resistance to flow was greatly increased during carbon dioxide inhalation when the patient was conscious. However, when the patient was anaesthetized, resist-

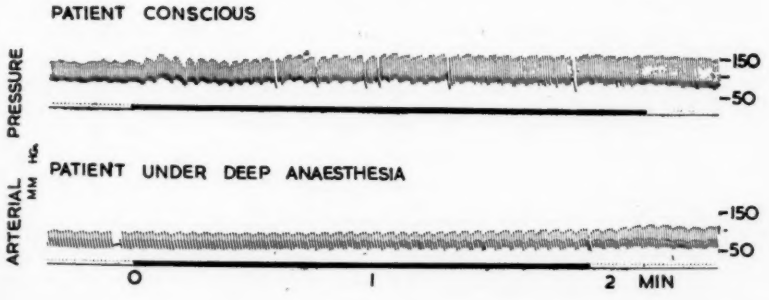

FIG. 2

A comparison of the effect of 30 per cent carbon dioxide inhalation on arterial blood pressure in the conscious and the anaesthetized patient.

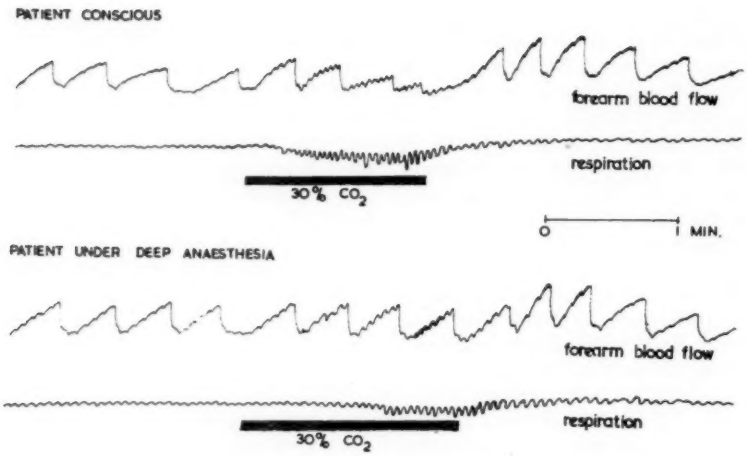

FIG. 3

Plethysmograms of forearm blood flow and stethographic tracings of respiratory excursion (inspiration downwards) during 30 per cent carbon dioxide inhalation made (*a*) when the patient was conscious (above), and (*b*) when the patient was anaesthetized (below). The black rectangles represent the periods of carbon dioxide inhalation.

TABLE I

The effect of anaesthesia on the changes in forearm blood flow with 30 per cent carbon dioxide inhalation.

	Forearm blood flow (ml/100 ml/min)					
	When conscious			When anaesthetized		
Patient	Before CO_2	During CO_2	Peak flow after CO_2	Before CO_2	During CO_2	Peak flow after CO_2
1	3.0	0.4	8.3	2.5	2.0	7.8
2	3.0	1.1	9.5	4.0	4.5	9.2
3	6.0	3.3	12.2	6.0	5.6	10.2
4	1.0	0.2	14.5	1.4	0.8	8.5
5	4.5	3.0	17.5	6.2	6.8	15.0
6	2.5	1.2	9.1	3.0	3.0	8.5
7	4.2	2.7	9.2	3.0	7.1	9.0

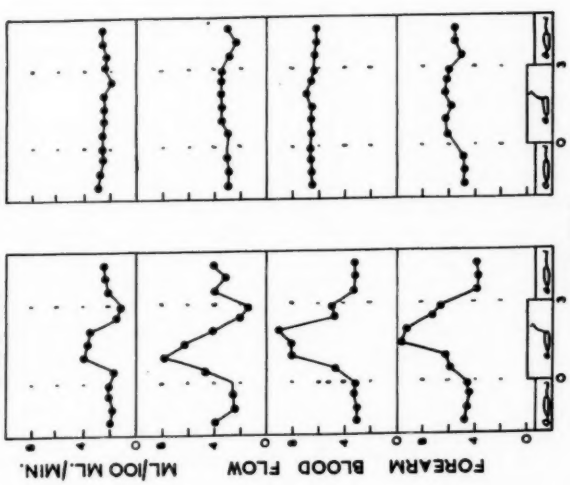

FIG. 5

The effect of general anaesthesia on the reflex vasodilatation in the forearm when the legs of a recumbent subject are passively raised. Left panel, patients conscious. Right panel, patients anaesthetized.

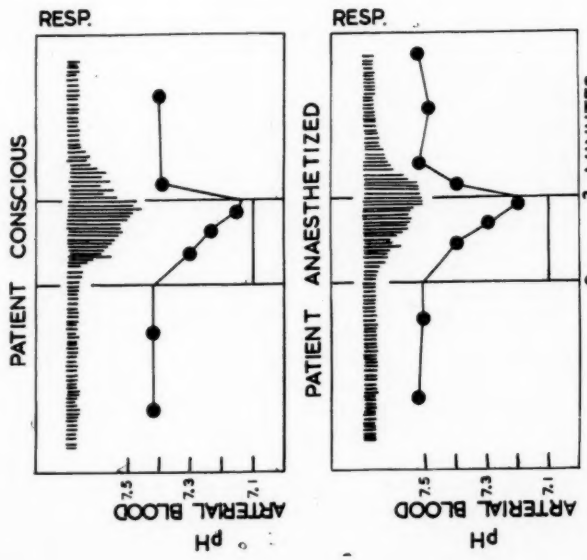

FIG. 4

A comparison of the fall in arterial blood pH during carbon dioxide inhalation in the conscious and anaesthetized patient.

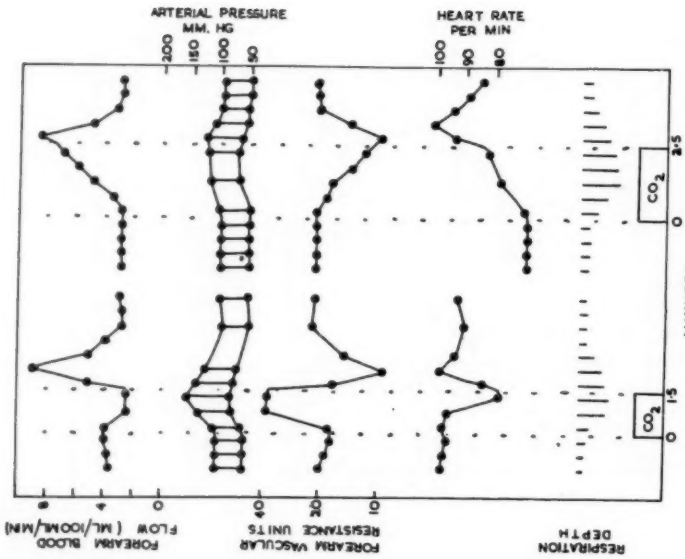

FIG. 7

The effect of general anaesthesia on the responses of forearm blood flow, arterial pressure, forearm vascular resistance, heart rate and ventilation (inspiration downwards) to inhalation of 30 per cent carbon dioxide in oxygen.

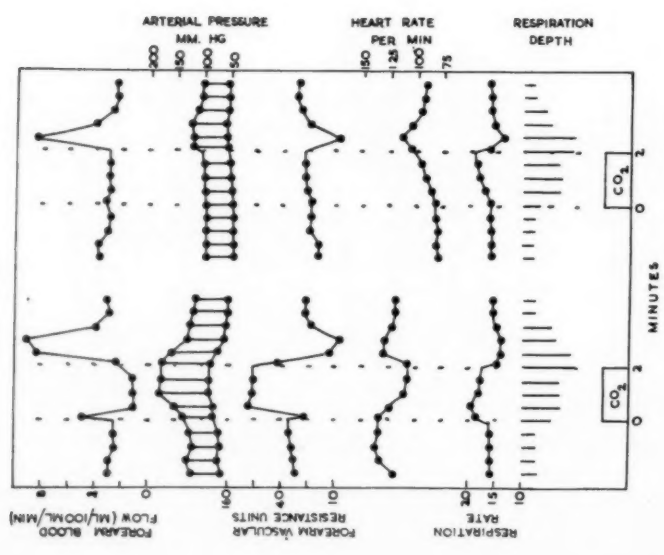

FIG. 6

The effect of general anaesthesia on the responses of forearm blood flow, arterial pressure, forearm vascular resistance, heart rate and ventilation (inspiration downwards) to inhalation of 30 per cent carbon dioxide in oxygen.

ance to flow in one case did not increase and in the other actually fell. These experiments also showed the effect of anaesthesia on the heart rate response. In the conscious patient the heart rate fell whereas in the anaesthetized patient it rose.

DISCUSSION

Vascular resistance changes.

Hypercapnia in man causes hypertension (Goldstein and Dubois, 1927; Dripps and Comroe, 1947; Lechtenbörger et al., 1954; Holmdahl, 1956) associated with vasoconstriction in the limbs, mainly in skeletal muscle (McArdle et al., 1957). Vasomotor nerves are largely responsible for the vasoconstriction when 30 per cent carbon dioxide is breathed since it is much less intense when the sympathetic nerves to the limbs have been blocked with local anaesthetic solution. However, even in the nerve-blocked limb, carbon dioxide inhalation causes a slight increase in resistance to blood flow. This is not due to the mechanical effects of the associated hyperpnoea, since even violent hyperpnoea does not affect resistance to blood flow in the forearm, provided carbon dioxide balance is maintained (Roddie, Shepherd and Whelan, 1957). The increase in resistance in the nerve-blocked forearm must therefore be due to a humoral mechanism, either some biochemical change in the blood, or to the release of some hormone causing vasoconstriction in skeletal muscle. There is evidence that hypercapnia causes an increase in the release of noradrenaline from the suprarenal glands (Dunér, 1955) and this substance is known to cause vasoconstriction in both skin and muscle (Duncanson, Stewart and Edholm, 1949; Swan, 1949; Barcroft and Konzett, 1949; De Largy et al., 1950).

In the present experiments when the patients were deeply anaesthetized, carbon dioxide inhalation either caused no change or a fall in forearm vascular resistance. This was not because the depression of the respiratory response to carbon dioxide with anaesthesia led to a smaller amount of carbon dioxide being taken up by the lungs than in the conscious patient. The fall in arterial blood pH during 30 per cent carbon dioxide inhalation was similar in the conscious and the anaesthetized patient. Other circulatory reflexes such as the forearm vasodilatation in response to change in posture (Roddie and Shepherd, 1958) were either greatly reduced or abolished, so that it is likely that the decrease in the vasoconstrictor response to carbon dioxide inhalation was part of a general depression of reflex activity by the anaesthetic drugs. The results would imply that both the nervous and humoral components of the vasoconstriction with hypercapnia were dependent on normal functioning of the nervous system.

In the patients where carbon dioxide inhalation caused a fall in forearm vascular resistance during anaesthesia, depression of the reflex vasoconstrictor response would not completely explain the results. It has long been postulated that carbon dioxide exerts two actions with opposite effects on peripheral vascular tone, a direct action causing vasodilatation (Anrep, 1912–13) and an indirect action due to direct and reflex stimulation of the vasomotor centres, causing vasoconstriction (Itami, 1912). When the central nervous system is intact, the indirect action is the dominant one. The present results could be explained by the hypothesis that general anaesthesia had so depressed reflex activity that the direct action of carbon dioxide became the dominant one, causing a fall in vascular resistance due to local vasodilatation. Though the direct effect of carbon dioxide on human muscle blood vessels is not known, there is evidence that it has a direct dilator effect on human cerebral vessels (Kety and Schmidt, 1948) and skin vessels (Diji and Greenfield, 1958; Blair, Glover and Greenfield, 1958).

A large transient vasodilatation occurs in the forearm within a few seconds of stopping carbon dioxide inhalation. A similar vasodilatation has been observed in the dog leg when artificial respiration is commenced after a period of apnoeic diffusion oxygenation (Holmdahl, 1956). During this procedure (ADO), carbon dioxide retention occurs, and when artificial respiration is started there is a rapid fall in the arterial blood P_{CO_2}. The exact mechanism of this vasodilatation is obscure, though it seems to be related to a rapidly falling P_{CO_2} in the arterial blood. It has been attributed to the sudden withdrawal of the indirect vasoconstrictor action of carbon dioxide, but this cannot be the whole explanation. The vasodilatation is frequently much greater than that obtained by full release of vasoconstrictor tone by nerve block. Further, even after the vasomotor nerves to the forearm have been blocked

the after-vasodilatation still occurs. Finally general anaesthesia, which greatly depresses the reflex vasoconstrictor response to hypercapnia, is without any noticeable effect on the after-vasodilatation. It would appear, therefore, that a humoral mechanism, related in some way to the rapidly falling arterial P_{CO_2}, is involved in the response.

Sudden reversal of the hypercapnic state frequently leads to hypotension both in dogs (Euler and Liljestrand, 1946) and in man (Dripps and Comroe, 1947; Holmdahl, 1956). It is probable that this fall in arterial pressure is due to the post-hypercapnic vasodilatation since there is evidence that the cardiac output tends to rise at this time (Holmdahl, 1956). The vasodilatation for the reasons mentioned above does not seem to be dependent on the nervous system. Therefore though anaesthesia may protect the patient from dangers of the pressor response to carbon dioxide inhalation, since this is largely mediated through the nervous system, it may not greatly modify the dangers of the post-hypercapnic state. It is in this immediate post-hypercapnic period that shock (Dripps, 1947) and severe cardiac irregularities (Brown and Miller, 1952) may occur.

When the face mask was placed over the conscious patient's mouth at the beginning of the carbon dioxide inhalation there was usually a transient small increase in forearm blood flow preceding the subsequent vasoconstriction. This vasodilatation did not occur in the anaesthetized patient and it is therefore likely that it was due to the apprehension associated with placing the mask on the face (Wilkins and Eichna, 1946).

Arterial pressure changes.

The pressor response to carbon dioxide was either greatly reduced or abolished by deep anaesthesia. This is in agreement with the findings in deeply anaesthetized patients during ADO (Enghoff, Holmdahl and Risholm, 1951). It can probably be explained by the depression of the reflex vasoconstrictor mechanism but other factors such as differences in the cardiac output response to carbon dioxide (Nahas and l'Allemand, 1956; Holmdahl, 1956) may have been operative. In relation to this point it is of interest that in the present experiments arterial pressure never fell in the anaesthetized patient during carbon dioxide inhalation even when there was a marked fall in forearm vascular resistance.

Heart rate changes.

Hypercapnia caused bradycardia in the conscious patient but this effect was reversed when the patient was deeply anaesthetized. We can think of no simple hypothesis to explain this. The action of carbon dioxide on the heart rate is complex but the bradycardia in the conscious patient might be explained by the effect of the raised arterial pressure on baroreceptors and the direct effect of hypercapnia on the heart (Andrus and Carter, 1924; Carter, Andrus and Dieuaide, 1924; Gesell, Mason and Brassfield, 1944). Vagal responses are enhanced by hypercapnia (Campbell, 1955; Holmdahl, 1956) and it has been suggested by Gesell, Mason and Brassfield (1944) that acid might act as a "physiological anticholinesterase". However, the bradycardia in dogs during ADO has been found to occur after division of the vagi (Nahas and l'Allemand, 1956). It is possible that the reversal of the normal heart rate response by deep anaesthesia was partly due to the general depression of reflex activity by the anaesthetic drugs, since it was found that other reflexes affecting heart rate were depressed. When the common carotid arteries were compressed in three patients (Roddie and Shepherd, 1957) tachycardia occurred. During deep anaesthesia, however, the increase in heart rate with carotid compression was either greatly reduced or absent in these patients.

Ventilatory changes.

Though assessment of ventilation was crude most of the present experiments confirmed that general anaesthesia depresses the respiratory response to carbon dioxide inhalation (Dripps and Dumke, 1943; Swerdlow, 1957; Swerdlow and Newman, 1957; Scurr, 1956). However, the depression of the respiratory responses seemed less marked than the depression of the vascular responses.

Anaesthesia and carbon dioxide balance.

Carbon dioxide accumulation in the body is not infrequently seen during general anaesthesia. Many factors such as the respiratory depressant action of anaesthetic drugs (Dripps and Dumke, 1943), the increase in respiratory dead space (Severinghaus and Stupfel, 1955; Pask, 1958), the

increased use of muscle-relaxants (Churchill-Davidson, 1958), the inefficiency of artificial ventilation (Gordon et al., 1951) and the use of hypothermia (Lucas, 1958) may be responsible for the resultant hypercapnia. The ill-effects of this respiratory acidosis have not been clearly defined but it has been suggested that some of the cardiovascular complications which may accompany anaesthesia are due in part to altered carbon dioxide balance (Dripps, 1947; Miller et al., 1952; Price, Connor and Dripps, 1953; Buckley et al., 1953). The present experiments show that general anaesthesia may greatly modify the normal cardiovascular responses to hypercapnia and this is a point which should be borne in mind whenever cardiovascular changes during anaesthesia are being attributed to changes in carbon dioxide elimination.

SUMMARY

(1) The vascular responses to breathing 30 per cent carbon dioxide in oxygen were compared during and after general anaesthesia.

(2) When the patient was conscious the inhalation caused marked hypertension and bradycardia and intense vasoconstriction in the limbs.

(3) When the patient was deeply anaesthetized these responses were greatly modified. The pressor response was greatly reduced and the heart rate rose slightly. Vascular resistance in the limbs was either unchanged or fell.

(4) Evidence was presented that the alterations in the responses during anaesthesia were due to a general depression of reflex activity by the anaesthetic drugs.

ACKNOWLEDGMENTS

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TWENTY YEARS OF CLINICAL NERVE BLOCKING*

BY

J. R. J. BEDDARD

Royal United Hospital, Bath, England

"The smoke stood up from Ludlow,
The mist blew off the Teme."
A. E. Housman, "A Shropshire Lad."

A M D G

HENRY HILL HICKMAN

Member of the Ryl. College of Surgeons

Born at Lady Halton in this Parish, Jan. 27
Baptized in this Church January 30, 1800
Died at TENBURY, April 2
Buried in this Churchyard
April 5, 1830

This tablet is placed here at the initiative of the Section of Anaesthetics of the Royal Society of Medicine as a Centenary Tribute to the memory of the earliest known pioneer of Anaesthesia by Inhalation.

Honour a Physician with the honour due unto him. A.D. 1930

Tablet in Bromfield Parish Church, near Ludlow, Salop.

IN the valley of the Teme, at the beginning of the last century, there was born a man who dedicated his life to the relief of pain. He became the apostle of anaesthesia, but first and foremost he was a clinical doctor treating sick patients and not a technician manipulating a machine.

This paper is being read because I believe that the importance of regional analgesia is appearing in the field of diagnosis and therapy. This is a fairly recent occurrence and leads the anaesthetist away from his stool in the theatre to the bedside, where his opinion is often of the greatest benefit to the patient and should be valued by both the physician and the surgeon. This departure from the theatre stool also occurs when patients are in need of artificial respiration by positive pressure, in which the anaesthetist plays a vital part. There are some, I suspect, who would like to class us as anaesthetic technologists and deny us our clinical birthright. We must be vigilant and live a full professional life.

For the purpose of this talk the term nerve block will be used in its widest sense and defined as the interruption of the nervous impulse at a given point in the lower motor neurone by means of an injection. It is hoped that this definition will leave the field wide open for discussion. The following classification will explain the types of nerve blocks that were used:

(A) TEMPORARY NERVE BLOCKS

(1) BLOCKS OF SHORT DURATION—up to three hours.
- (*a*) Surgical Analgesia.
- (*b*) Diagnostic nerve blocks.
- (*c*) Therapeutic nerve blocks.

Drugs used: Procaine, Amethocaine, lignocaine.

(2) BLOCKS OF LONG DURATION—up to several days.
Therapeutic.

Drugs used: Proctocaine, Efocaine.

(B) PERMANENT NERVE BLOCKS

Therapeutic.

Indications:

(1) Intractable pain (usually incurable cancer).
- (*a*) Chemical neurotomy.
- (*b*) Subarachnoid injection.

Drugs used: Aqueous phenol, alcohol, phenol in glycerine, silver nitrate in glycerine, phenol in Myodil.

(2) Circulatory failure.
Chemical sympathectomy.

Drugs used: Phenol in aqueous solution.

It is now nearly twenty years since I first became interested in nerve blocking: there have been times of satisfaction with a sense of achievement, and times of acute anxiety.

In 1942 I attended a demonstration by Dr. N. R. James at the West Middlesex Hospital and was so impressed that I decided to give his techniques a trial. My opportunity came a year later

* Paper given to a meeting of the Society of Anaesthetists of the South-Western region at Bath, May 1958.

on being posted to a military hospital in West Africa. I performed a series of 552 nerve blocks and then submitted a paper via the War Office for publication. The paper was never published on account of the shortage at that time of printing paper. On reading it through again, I find I listed the following advantages:

1. The patient had immediate relief from pain, which lasted for a period of up to four hours.
2. The patient was conscious and co-operative, requiring no postanaesthetic care.
3. Traumatic shock due to painful stimuli was arrested.
4. Muscular relaxation was found to be equal to that of spinal subarachnoid analgesia.
5. The presence of the anaesthetist was not usually required for anaesthetic purposes in the theatre, and he could do several nerve blocks while the surgeon was attending to one case. On one occasion, under emergency conditions he was able to keep several surgeons continually supplied with cases ready for operation.
6. In contrast to spinal analgesia there was no fall in blood pressure, no risk of meningitis, and headaches did not occur. In 552 cases no infection occurred at the site of injection.
7. The apparatus is light and easily portable.
8. When a Medical Officer is alone in an isolated part of the world, he can give the nerve block and then proceed with the operation without hurry and without any anxiety about the anaesthetic condition of the patient—a point which will be appreciated by members of the army and other medical services overseas.

The advances in other methods of anaesthesia have been very considerable since those words were written. We now have relaxants, hypotension, and hypothermia; and the modern general anaesthetic is usually though not always the method of choice today. Hence, the indications for regional analgesia have been narrowed by the excellence of present-day methods, but if adrenaline is left out of the local analgesic solution, regional block is still a first-class technique for operations on the elderly and moribund cases and when vomiting is a complication to be feared or it is known that the patient has recently had a large meal. I have recently used nerve block analgesia with great success for orthopaedic operations to pin the neck of the femur in senile patients with auricular fibrillation and chronic chests. Sometimes the simplest of nerve blocks will save the anaesthetist a lot of worry and anxiety. Not long ago I was asked to give an anaesthetic to a young man who was lying on the trolley in great pain with a fracture of the right femur at the junction of the upper and middle thirds of the shaft. The X-ray photograph showed that the upper fragment was flexed at the hip and the lower fragment was overlapping posteriorly; I believe this is quite a common displacement. The patient was lying in the dorsal position, and his pulse rate was 126 beats per minute. All it was necessary to do was to expose the inguinal region and inject the femoral nerve half an inch below the inguinal ligament; the lateral cutaneous nerve was similarly injected. In five minutes all pain had gone, the pulse rate had dropped to 74 beats per minute and the patient had become quite chatty. The surgeon was able to reduce the fracture and put the limb up in extension without causing any discomfort, and the patient was able to digest his meal in peace. It was assumed that in this type of fracture the pain path travels to the central nervous system via the femoral nerve. Those who do regional nerve blocks should attempt to reason out the "pain paths" in each case that they encounter and not rely wholly on routine techniques which may in certain cases lead to either excessive or insufficient injection. In other words one must think of the patient and not of the technique. The latter will come automatically after a short period of practice. Another nerve block which might be useful to the orthopaedic surgeon is the block of the hand at the level of the wrist joint. This will allow a painless voluntary movement of the fingers by the muscles of the forearm even if the tendons are exposed in the hand. If active movements are desirable in a painful condition of the hand they can be painlessly encouraged under a series of wrist nerve blocks. In West Africa we were several times successful in freeing flexor tendons of adhesions by the use of this block combined with active movements.

Temporary long acting local anaesthetic drugs, such as Proctocaine and Efocaine have in my practice proved disappointing. They are often irritating to the tissues and the length of action claimed for them is open to suspicion and is very variable. The lateral cutaneous nerve of the thigh was blocked with Proctocaine and sensitivity to pinprick returned within twenty-four hours. The duration of these drugs was also disappointing in stellate ganglion block where Horner's syndrome passed off as early as two hours after injection. A patient suffering from a local painful neurosis

(neurologist's diagnosis) of the temporal region received a second injection of Proctocaine 5 ml on May 26, 1954, with the result that an extensive angioneurotic oedema of the same side of the face and neck started to develop forthwith. It was feared that an oedema of the glottis might develop and she was admitted to hospital where the condition was successfully treated. If a really reliable, nonirritating, long acting, temporary local anaesthetic drug could be synthesized the treatment of many painful conditions could be revolutionized.

Permanent nerve blocks are used in certain cases of intractable pain and for chemical sympathectomy. Perhaps the most controversial aspect of this subject is the use of permanent nerve blocks for the relief of the pain of incurable malignant disease. The drugs used are usually either alcohol or phenol. Since 1951 attempts have been made in the Radiotherapy Department of this hospital to ease the intolerable pain of advanced cancer by means of permanent nerve block analgesia. At first attempts were made to cut off the sensation of the painful part of the body from the c.n.s. by means of chemical neurotomy. The nerves from the painful area were chemically divided by a nerve block consisting of a small quantity of phenol, sometimes in watery suspension and sometimes dissolved in spirit. Spirit was soon discarded as a solvent as it was noticed, in the case of nerve trunks, that a neuritis, presumably of the proximal part of the severed nerve was a frequent sequela. However, some good results were obtained by using an aqueous suspension of up to 40 per cent phenol in injections of 2 ml. Not more than two injections were made at one time, and if necessary further injections were made after a week. Apart from mechanical paraesthesiae, the injections themselves were always painless and there was no sloughing of the skin as superficial injection was avoided.

About this time my attention was drawn to an article by Ansbro (1950) entitled "Intraspinal Segmental Alcohol Block for the Relief of Intractable Pain". A Tuohy catheter with a stylet in place was passed through a Huber pointed needle in the lumbar spine and advanced in the subarachnoid space to the desired height. The exact position was checked radiographically and 0.5 to 1.0 ml. of absolute alcohol was deposited around the sensory roots supplying the painful area. It took months to procure a Tuohy catheter and Huber pointed needle from America, and then the technique was tried out once on a patient extremely ill with incurable carcinoma of the lung. Unfortunately the catheter became coiled up in the subarachnoid and was not withdrawn without trauma. I am afraid this was because an attempt was made to advance the catheter farther up the subarachnoid space with the stylet removed. Another point to remember is that the catheter must not be withdrawn back through the Huber pointed needle. If this is attempted there is danger of cutting the catheter off with the point of the needle and leaving part in the subarachnoid space. They must be withdrawn together. This latter pitfall was foreseen and avoided.

In January 1955 Maher published his paper entitled "Relief of Incurable Pain in Cancer". Intraspinal segmental alcohol was put on one side in favour of Dr. Maher's simpler technique of subarachnoid phenol and silver nitrate in glycerine. Chemical neurotomy was reserved for cases in which the growth involved the cranial nerves where subarachnoid injection of the sensory roots was impossible.

To illustrate chemical neurotomy, I am going to quote from the notes of two cases of incurable carcinoma in the cranial nerve area. The first case was a woman whom I treated in 1951; she was suffering from an epithelioma of the tongue invading the floor of the mouth and the mandible. The patient had very severe pain related to the area of the third division of the trigeminal nerve. The third division was blocked via the masseteric notch with 2 ml of 10 per cent phenol in aqueous solution. The patient had relief of pain and lived for eleven weeks, dying from pneumonia.

The second case was an elderly woman with an epithelioma of the upper right eyelid. She came for chemical neurotomy on July 16, 1951, when she had an obvious secondary in the pre-auricular glands and the pain appeared to be referred to the area supplied by the auriculo-temporal nerve. A similar block of the third division of the fifth nerve was carried out using 10 per cent phenol. On August 8, 1951, the pain recurred in the right ear and also in the supra-orbital region. Injection of the gasserian ganglion using 1 ml of 10 per cent aqueous phenol was carried out. One month

later there was a slight return of pain in the right eye and ear. The infra-orbital region was insensitive to pinprick.

On September 22, 1951, the pain was severe and a second injection into the gasserian ganglion was made.

On October 2, 1951, the patient complained of a little pain in the right eye but this was quite bearable.

On October 23, 1951, the pain in the ear was better, but the pain in the right eye was worse.

On October 30, 1951, the gasserian ganglion injection was repeated for the third time, using 1 ml of 10 per cent phenol in spirit. The patient was free from pain.

On January 29, 1952, she still had some pain but it was easily controlled with tablets. The general condition was deteriorating and no further injection was considered advisable.

On February 2, 1952, the patient died.

This may not appear to be a very successful case, but on February 4, 1952, we received an unsolicited letter from the patient's general practitioner which threw some light on the domiciliary side of the picture.

> You will be glad to know that Mrs. X passed away on Saturday morning last. Thanks to the treatment given we were able to keep her relatively free from pain. Her general condition had been deteriorating for two to three weeks, but it was only the last 48 hours that she was unable to be about.

As a general rule Maher's subarachnoid technique with phenol and glycerine has advantages over chemical neurotomy where spinal nerves are concerned, for with subarachnoid injection it is possible to position the patient so that only the sensory dorsal roots are attacked, leaving the motor roots unaffected. Phenol and glycerine appears to be a better drug than alcohol as it can be more easily confined to a few spinal segments. However, in some cases there was slight motor weakness and in pelvic cases often a loss of bladder control. Another troublesome side effect happened occasionally; this was a "girdle pain" of hyperaesthesia which occurred on the edge of the numb area. This usually resolved in a day or two and was treated expectantly with tabs. codeine co and tabs. benerva co. I think this might be brought about by irritation due to the glycerine or alcohol. This observation prompts me to mention another solvent for the phenol, namely, Myodil, as so far I have not noticed any "girdle pains" when using phenol in this solvent. In the *Lancet* of January 11, 1958, an article entitled "Intrathecal Phenol for Intractable Pain" by Drs. Nathan and Scott describes the advantages of using phenol 7.5 per cent in Myodil. So far I have used it in two cases of pelvic incurable cancer with good results and without any "girdle pains" and without any interference with micturition or defaecation. I attribute this to the fact that Myodil is less viscous and less irritating than glycerine with its hygroscopic action. I now use phenol in Myodil combined with Maher's technique for all incurable malignant pain in the spinal area. Since 1951 about 80 cases have been treated by permanent nerve block so that it is now possible to consider the data which should guide the anaesthetist in deciding upon this procedure.

(1) One must be absolutely certain that the patient is suffering from advanced malignant disease and that this is the cause of his pain.

(2) The time in the illness for the injection must be carefully considered. The patient must have intolerable and continual pain. He should be referred for therapy when analgesics such as tabs. codeine co. are no longer effective, but before the habit forming opiates are given. A patient addicted to morphia, etc., will crave for the drug and in order to get more morphia lie about his pain. The main advantage of permanent nerve block is that many weeks of drug addiction can be avoided and the patient can live comfortably at home. Morphia and allied drugs should be reserved for the terminal stages.

(3) The patient should have an expectation of life of more than three weeks. If the patient is about to die, euphoria with systemic drugs may be preferable.

(4) It is well to remember that in most people the memory for pain which has been relieved is very short, and often a patient who has been relieved of his acute pain will complain bitterly about the numb dead feeling in the area affected by the injection.

(5) The area of analgesia tends to shrink with the passage of time. This is most noticed in the first five days after injection.

(6) As time goes on the malignant condition

may disseminate and extend locally invading tissues outside the area of analgesia, or metastases may cause pain in a different part of the body. It is then necessary to review the case and decide whether further injection is indicated or the time for euphoria has arrived.

(7) The patient must first be told about the action of the injection. He must understand that, although his intolerable pain will be greatly eased and that he will be able to sleep and move about more easily, he will rapidly forget how bad it all was and will complain about the area of numbness which he is having instead of the pain.

(8) It is advisable to ask him to sign a form that he agrees to have the injection which has been fully explained to him. His signature should be witnessed by a responsible third party.

It is very difficult to assess the success and degree of relief of pain in these cases. Nearly all appear to be helped. A successful case will sleep naturally, and it is noticed that the patient's facial expression improves. Instead of looking drawn and haggard, he looks fresh and is more cheerful, though as time goes on he will feel weaker and may say that although his pain is much better, he feels ill. Taking all the points into consideration the palliative treatment of the pain of incurable cancer by nerve block is probably the best help that can, at present, be offered to these dying patients. It is to be hoped that improvement in the treatment of malignant disease will soon make relief of incurable cancer pain by nerve block redundant.

Chemical sympathectomy is another form of permanent nerve block. I use the technique in which 10 per cent phenol in aqueous solution is injected into the region of the second and third lumbar sympathetic ganglia using 5 ml for each ganglion. Many cases have been done. They are generally cases of arteriosclerosis with failing circulation and threatened gangrene. Cases are referred for chemical sympathectomy by the orthopaedic, medical, and surgical faculties. The results are most encouraging where arterial and venous spasm is a factor. Even in cases where endarteritis obliterans is the main factor there is sometimes a small degree of associated spasm, and chemical sympathectomy is worth a trial. In this type of case it is seldom worth while performing a preliminary temporary sympathectomy with a short acting local anaesthetic. The improvement in the nutrition of the tissues may take several days to make itself apparent, and a short acting local anaesthetic such as procaine and amethocaine will have been eliminated long before the tissues have time to show any improvement. A trial temporary sympathectomy can be most misleading. The results of chemical sympathectomy for intermittent claudication have not been impressive.

The nonmedullated nerve fibres are very susceptible to phenol and a very accurate destruction of the lumbar sympathetic is obtained. The cases referred to one are usually aged people with advanced arteriosclerosis which are considered unsuitable for surgical operation. It is much more difficult to get good results with the surgically unfit, and so one wonders whether in time chemical sympathectomy will replace the operation of lumbar sympathectomy. Chemical sympathectomy is a practically painless procedure and the patient need only be in hospital for twenty-four hours. In a few cases a tiresome neuralgia, referred mainly to Scarpa's triangle may follow chemical sympathectomy. The hyperaesthesia is usually referred to the area supplied by the genitocrural nerve which passes close to the sympathetic chain. The condition usually clears up in about six or eight weeks. This complication has not occurred recently, and it is thought that this is because the injections have been made farther forward on the bodies of the lumbar vertebrae concerned.

Chemical sympathectomy is contra-indicated when patients are being treated with anticoagulants as these spread the necrosive action of the phenol. In one case the greater part of the psoas muscle was found gangrenous at autopsy.

CONCLUSION

Twenty years ago clinical nerve blocking was performed by a few anaesthetists for analgesia in surgical operations. It was regarded as a safe but rather unreliable method for the relief of surgical pain, though with a little practice it became reliable.

Dr. N. R. James clearly demonstrated its safety and reliability when he was working at the West Middlesex Hospital. More recently, modern anaesthetic methods have tended to reduce the

need for surgical analgesia by nerve blocks, but a new scope has been demonstrated in the diagnostic and therapeutic field, making demands on the anaesthetist's ability as a clinical doctor.

ACKNOWLEDGMENTS

In closing I express my thanks to Dr. A. A. G. Fleming, Consultant Radio-Therapeutist, Bath, who has provided me with cases, lent me beds, and given me encouragement in times of difficulty. Also to the Orthopaedic, Medical, Gynaecological, and Surgical Faculties who have referred cases for diagnostic and therapeutic nerve block.

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ACCIDENTAL INTRA-ARTERIAL ADMINISTRATION OF THIOPENTONE ON THE BACK OF THE HAND

BY

THOMAS W. BAILLIE

University Department of Anaesthesia, Glasgow Royal Infirmary, Scotland.

THIOPENTONE sodium was first introduced into anaesthetic practice in 1934 as Pentothal Sodium by J. S. Lundy of the Mayo clinic.

One of the hazards associated with the administration of this drug is that of intra-arterial injection, of which many instances have now been recorded. The frequency of this accident has been estimated recently as one intra-arterial injection in about every 3,500 administrations of thiopentone sodium (Dundee, 1956).

Intra-arterial injection of thiopentone results most commonly from attempted intravenous administration in the region of the antecubital fossa. In consequence, it is now commonly agreed that injection of thiopentone in this area is better avoided; indeed, some workers state that the dorsum of the hand should be the site of choice for such injections (Forrester and Saunders, 1955) on the supposition that the back of the hand contains no superficial arteries.

The purpose of this report is to stress that intravenous injections of thiopentone in the dorsum of the hand must be carried out with the degree of care that would be exercised when injecting the drug in the antecubital region, since a superficial artery may also be punctured there.

CASE 1

A healthy woman aged 32 years, was presented for surgical treatment of bilateral varicose veins on February 24, 1958. Premedication consisted of papaveretum 22 mg and scopolamine 0.43 mg. Manual compression was applied to the right wrist in order to display the veins on the dorsum of the hand and a vessel was selected for administration of thiopentone. An initial dose of 1.5 ml of 5 per cent thiopentone was given and almost immediately the patient complained of agonizing, burning pain in the wrist and hand and attempted to pull away the limb. At the same time there appeared an intense blanching of the ulnar two-thirds of the dorsum of the hand and of the proximal dorsal surfaces of the medial three fingers.

Taking care to leave the needle in situ, the syringe was detached and the remainder of the 500 mg thiopentone injected into the contralateral forearm. Five ml of 1 per cent procaine was injected into the artery which had been entered inadvertently and the surrounding subcutaneous tissue was infiltrated with a further few millilitres of the same solution. Within 10 minutes, the intense blanching was replaced by a reactive hyperaemia. Heparinization was not carried out and the surgical procedure was performed under nitrous oxide and oxygen anaesthesia with intermittent intravenous pethidine.

Postoperatively, the patient had no discomfort or pain. Furthermore, postoperative examination revealed no obvious pulsation on the dorsum of the right hand.

CASE 2

On June 4, 1958, a 63-year-old woman received papaveretum and scopolamine in the same dosage as above in preparation for biopsy of axillary lymph glands under general anaesthesia. Whilst commencing the intravenous injection of thiopentone it was noted that only a centimetre on the radial side of the venepuncture, an artery of appreciable size was pulsating clearly and visibly in the superficial tissues of the dorsum of the left hand for a distance of about 4 cm. The pulsations of this vessel could be appreciated readily on palpation by the author s assistant and the nursing staff.

Pulsation was difficult to obtain on the following day when the limbs were cooler and no longer under the vasodilating influence of the drugs used in premedication but the vessel could be discerned readily once vasodilatation had been produced by immersing the hand and forearm in hot water.

DISCUSSION AND COMMENT

Several excellent papers have already dealt with the incidence, pathology, prevention and treatment of inadvertent intra-arterial injection of thiopentone (Cohen, 1948; Stuart, 1955; Forrester and Saunders, 1956; Dundee, 1956).

The dorsum of the hand has been recommended as the site of choice for intravenous administration of thiopentone solutions on the

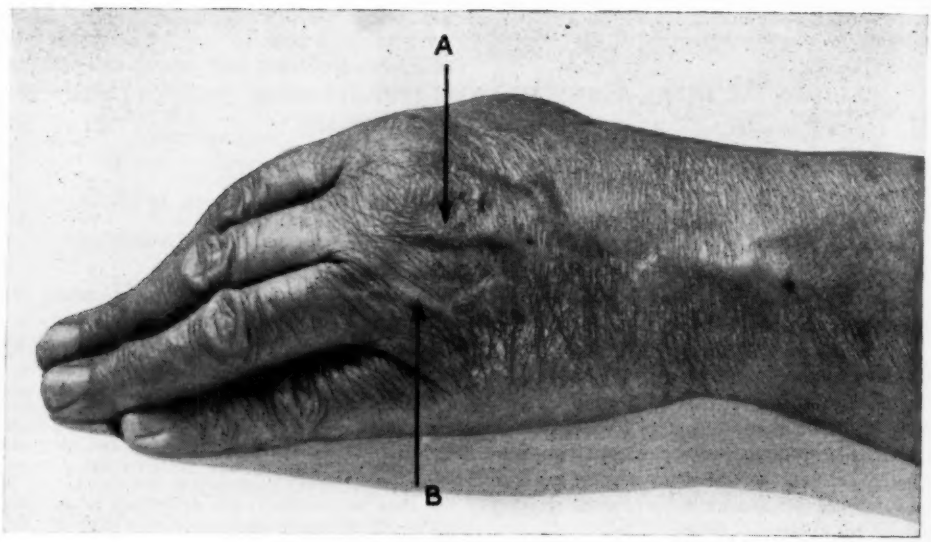

FIG. 1

Case 2. I. McG., aged 63 years.
A. Indicates site of pulsating artery. B. Indicates site of venepuncture.

basis that one is unlikely to encounter an arterial vessel in the superficial tissues of that region. The two cases above indicate that such vessels do exist in that area, probably branches of the dorsal metacarpal arteries from the posterior carpal arch or of the perforating intermetacarpal branches of the deep palmar arch.

When such vessels do exist their presence may not be detected as very little compression with a "venous" tourniquet readily causes pulsation to cease. It must be stressed, therefore, that careful examination of the dorsum of the hand should be performed before application of a manual or other tourniquet to the wrist.

It is possible that intra-arterial injection of an irritant drug in this area is less likely to carry the disastrous consequences of such an injection higher in the arm, firstly because the main limb of a major artery supplying a large area is spared and secondly, because the main arterial supply to the hand and digits is derived from the arterial arches of the palmar aspect. There can be no doubt whatsoever that the use of a 2.5 per cent solution of thiopentone will lessen still further the likelihood of serious damage to the hand or fingers should this mishap occur.

ACKNOWLEDGMENTS

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PETHIDINE-PROMAZINE SUPPLEMENTATION OF REGIONAL ANALGESIA

A Preliminary Communication

BY

MARK SWERDLOW AND E. C. COCKINGS

Salford Royal Hospital, Manchester, England

It has long been common practice to render the patient drowsy or asleep when spinal, epidural or other form of regional anaesthesia is employed. For many years opiates were usually employed for this purpose—morphia, heroin, and papaveretum each having its advocates. When these drugs were administered in small dosage the patient was frequently much too alert: when large doses were employed, nausea, respiratory depression and other unwanted effects ensued.

More recently the usual practice has been to keep the patient lightly asleep by intermittent injections of thiopentone. Such a use of thiopentone is not without its drawbacks. Unconsciousness will be followed by the loss of laryngeal and pharyngeal reflexes and the need to maintain an airway. In the young and fit an undesirably large total amount of thiopentone may be required with delay in recovery of full consciousness. Should analgesia be in the least imperfect the patient under thiopentone will respond and "a little thiopentone" will become a full anaesthetic—the patient in fact receiving two anaesthetics for one operation.

In this report we present briefly a method of supplementation which seems to have advantages over these previously employed.

MATERIAL AND METHOD

Tranquilizer drugs appear to offer a useful means of rendering the patient lightly unconscious whilst being operated on under regional analgesia. It was decided to investigate the use of promazine (Sparine) for this purpose. Promazine hydrochloride is 10, 3,-dimethylamino-n-propyl phenothiazine hydrochloride.

We have now employed promazine supplementation in 75 cases who were undergoing operation under spinal, epidural, caudal, or refrigeration analgesia or under local block; the majority were elderly men undergoing genito-urinary operations.

The patients were premedicated with morphia 8–11 mg (according to size and age) and atropine 0.64 mg given subcutaneously about one hour prior to operation. All patients were adults.

In the initial cases promazine alone was injected intravenously after the regional anaesthesia had been instituted. This method did not prove consistently satisfactory. It appeared that promazine potentiated the morphia of the premedication; only if the latter was well timed and in relatively large dosage for the particular patient would light sleep ensue.

It was therefore decided to administer pethidine together with promazine, a mixture containing 25 mg of each drug per ml being employed. An initial dose of 1 ml was given and further doses of 1 ml each were given if necessary after intervals of observation of not less than 5 minutes. Two or three ml of this mixture almost invariably rendered the patient lightly asleep.

Using this 50:50 mixture of promazine and pethidine, it was noted that there was frequently a prolonged period of postoperative drowsiness during which the patient could be aroused and would co-operate on command but would lapse into sleep when left undisturbed.

In order to avoid this prolonged sleepiness, we have employed in our more recent cases a mixture of pethidine and promazine in a 2:1 ratio, each 1 ml containing 25 mg of pethidine and 12.5 mg of promazine. This mixture, in a dosage of 1–4 ml, equally consistently produces sleep but prolonged postoperative drowsiness is avoided. One or two ml of the mixture are usually given before

the regional block is performed and a further dose (or doses) given after the block has been completed.

The patient retains control of upper respiratory reflexes and maintains his own airway. Respirations remain adequate throughout; the skin is warm, pink and dry. Care must be taken to avoid sudden movement, tilting or rough handling lest a marked fall in blood pressure result. If blood loss occurs during operation, it should be replaced at once. It is important that the regional analgesia should adequately cover the field of operation.

At the end of operation the patients frequently wake on being moved to the trolley and can always be awakened by command or light tactile stimulation. On return to the ward they co-operate readily with nursing and physiotherapy measures. When questioned some time after operation, there is usually amnesia for the whole or most part of the operative period. Very frequently the patient does not even remember the regional block being performed. An added theoretical advantage is that the incidence of post-operative nausea and vomiting should be reduced by means of the promazine.

We have found this method uniformly satisfactory and now use it routinely when regional analgesia is being employed. It is hoped to present a detailed report of a large series of cases at a later date.

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A RARE TOXIC EFFECT OF LOCAL ANAESTHESIA WITH LIGNOCAINE

A Case Report

BY

JACK A. GOLDMAN

The Department of Obstetrics and Gynaecology,
The Beilinson Hospital, Petach-Tiqvah, Israel

METHODS of anaesthesia and analgesia in labour and delivery are varied and multiple. The problem of combining safety of mother and child with an effective method of pain relief is a rather difficult one to solve. So far no ideal method has been found.

Among other methods of anaesthesia for delivery, we use local anaesthesia of the pelvic floor in the form of a pudendal nerve block, with lignocaine (Esracaine brand) with considerable success.

In the many years in which local anaesthetic drugs have been in general use, toxic manifestations have frequently been reported (Sadove, 1952; Steinhaus, 1957).

They have been roughly classified into:

(1) Central nervous system effects, namely stimulation of the cerebral cortex and depression of the medulla.
(2) Peripheral effects, those affecting cardiovascular and respiratory systems.
(3) Allergic responses.

Psychic disturbance is not one of the well-recognized side-effects. We have been able to find only one such case described in detail (Bennett, 1957) and therefore believe that its occurrence is sufficiently rare to warrant publication of this report.

CASE REPORT

S. S., a 34-year-old woman, was admitted to the obstetrical department of the Beilinson Hospital in active labour, approximately at term of her first pregnancy.

On admission, physical examination revealed a well developed, small, rather thin woman in her 9th month of gestation. She was in good general condition, having fair uterine contractions at 5-minute intervals.

The antepartum period was essentially normal and all the laboratory data were within normal limits. There was no history of previous illness or fits. Menstrual history was normal.

After 8 hours of active labour, rectal examination revealed the uterine cervix to be fully dilated, but contractions had grown weaker. Two hours later the foetal head was still resting on the perineum. In view of secondary uterine inertia it was decided to aid by performing an outlet forceps delivery. Consequently, a pudendal nerve block with 1 per cent lignocaine solution with hyaluronidase was performed.

As soon as the needle was removed from the perineal skin, a mild twitching of the eyelids and facial muscles was noticed. The twitching became more pronounced and the facial muscles grew more tense and rigid. The patient's jaw was set and she failed to respond to questions. Slight cyanosis of the face supervened. However, during this time, the trunk, arms and legs remained relaxed. Tendon reflexes remained normal and not exaggerated. The pulse rate was slightly more rapid than before and the systolic and diastolic blood pressures were only ten points elevated, i.e. to 130/90 mm Hg. Oxygen was immediately administered and an intravenous barbiturate given. Outlet forceps delivery was done and a living baby girl in good condition was extracted.

Approximately 3 minutes after it had started, this "state of irritation" of her face as well as the muscle rigidity were controlled and subsided partly. Nevertheless, slight muscle twitchings continued and the patient grimaced for at least 3 more minutes. The patient then exhibited marked mental excitement. She repeatedly announced that she was going to die. When the baby was shown to her she paid no attention. She complained that her tongue was paralyzed and that this paralysis was going to last exactly 1 hour, since it had to move down her body and into her legs. Every statement was repeated several times.

At this point she became resentful and argumentative, and displayed signs of disorientation. For the next three or four hours the patient remained under close observation. Her predominant mood was one of euphoria; she became talkative and displayed a zest for conversation. Gradually she became relaxed and finally fell asleep.

On the following day the patient appeared perfectly rational and displayed a considerable insight into the happenings of the previous day. She recited to us everything she had said or done. When asked to describe what she had felt during the delivery she stated that she had realized something important was happening, though she could not say what. After a short period of confusion she at first had a feeling of impending doom, later felt "something beyond her control" forcing her to talk.

It is interesting to note that the patient had heard everything that was said in the room and had realized her mental confusion, yet was unable to control her behaviour.

COMMENT

This is a report of temporary psychic changes, which developed during administration of a pudendal nerve block anaesthesia with lignocaine for delivery.

Lignocaine (diethylaminoacet-2-6-xylidide hydrochloride) is a highly desirable local anaesthetic agent, according to Goodman and Gilman (1955). Since its synthesis by Lofgren and Lundquist (1946), it has steadily gained in popularity. Many authors (Gordh, 1949; Wiedling, 1952) have demonstrated its superiority to procaine in a number of properties; higher stability, lower incidence of side-effects and irritation, longer-lasting anaesthesia and higher potency. Sung and Truant (1954) studied the physiology and metabolism of lignocaine as compared to procaine and concluded that the first was superior.

Nevertheless, in spite of the paucity of reported reactions with this drug (Gordh, 1948, in a study of 800 cases who received lignocaine anaesthesia, has reported only two cases of convulsions; Dutton, 1955, has reported one case of convulsions after pudendal block), it may cause systemic toxic effects. Goodman and Gilman (1955) consider the drug as having approximately the same toxicity as procaine in 0.5 per cent solution; yet in 1 per cent solution it is 40 per cent and as 2 per cent it is 50 per cent more toxic than procaine. Hunter (1951), however, considers the drug twice as toxic as procaine in cats, mice, rabbits and white rats. It has also been said that "the toxicity of a local anaesthetic drug increases in geometrical, not arithmetical, progression with increase in concentration" (Betlach, 1941; Sadove, 1952).

Others believe this drug to be two to four times as safe as procaine (Carnegie and Hewer, 1950). Nevertheless, the total amount of lignocaine that may be injected has been fixed at 0.5 g. when used with epinephrine (Moore, 1953; *New and Nonofficial Remedies*, 1956). The maximal dose, according to others is 8 mg/kg (Martindale, 1952); the toxic dose, therefore, should be considerably in excess of this figure. Since our patient weighed 54 kg, the maximal dose given to her should have been 432 mg.

At the obstetrical department of the Beilinson Hospital we use approximately 50 ml of a 1 per cent solution of lignocaine for the pudendal block. The total amount given, therefore, was 500 mg, i.e. 68 mg more than the maximal dose according to body weight, but not more than the dose recommended by Moore (1955) and others, and by usually accepted standards would not have been expected to produce a toxic reaction. In analyzing our case we came to the conclusion that the factors which may have contributed were the following:

(1) The addition of 1500 I.U. Hyalase (hyaluronidase) which increases the diffusion of the anaesthetic solution, and may thus increase the rate of absorption.

(2) Failure to add to the solution adrenaline which decreases the rate of absorption by vasoconstriction.

(3) No sedation had been given during labour.

It is evident that the two first factors contribute to increase the rate of absorption of the drug and consequently favour the establishment of a high blood level (Collins, 1952), which in our case led to a toxic reaction.

Eclamptic convulsion in this case was excluded according to the clinical picture of the seizure, and after thorough investigation.

Although the evidence implicating lignocaine is not definite, we believe that the temporary mental changes of our patient are compatible with a toxic effect. Also, there was no previous history of mental aberration or instability. Further proof may be that the disturbance started with a convulsion, which is known to be a toxic side-effect of local anaesthetics. We feel, therefore, that the subsequent mental changes were manifestations of cortical cerebral stimulation, brought on directly by the local anaesthetic, lignocaine.

SUMMARY

A rare case of short psychic disturbances due to a toxic effect from Esracaine brand of lignocaine has been described. The possible contributing factors have been discussed.

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A TECHNIQUE OF ANAESTHESIA FOR THE OPERATIONS OF MYRINGOPLASTY AND TYMPANOPLASTY

BY

N. AIDAN VINCENT

Rotherham Hospitals and Montagu Hospital, Mexborough, England

IN recent years new techniques have been described in the surgical treatment of chronic suppurative otitis media. These new operations originally described by Zöllner (1951) and Wüllstein (1952) in Germany are plastic operations and differ from the old radical mastoid operation, as they are designed not only to remove all disease in chronic suppurative otitis media, but also, by means of a plastic procedure, to reconstruct the tympanum in such a way that useful and, in many cases, good hearing results. The old radical mastoid operation usually destroyed useful hearing as it was a purely destructive operation.

These operations are generally performed on infected and thus highly vascular temporal bones and as skin grafting is an essential part of the technique they have presented an anaesthetic problem in the control, with safety, of haemostasis greater than that presented in fenestration surgery.

Above 200 of these operations have been performed by Beales (1957, 1958) and the following anaesthetic technique has been evolved for these cases which have been performed at the Doncaster Royal Infirmary, Montagu Hospital, Mexborough and The Victoria Hospital, Worksop.

OPERATIONS

(a) *Myringoplasty.*

This is a simple repair of a perforated membrane when there is no middle ear disease and an intact and functioning ossicular chain.

The operation, which is carried out by the endaural approach, consists essentially in the application of a free full-thickness skin graft to the tympanic membrane after its superficial layer of skin has been removed. The operation is carried out using a binocular dissection microscope, and takes about 45 minutes. Haemostasis is essential for a successful "take" of the skin graft.

(b) *Tympanoplasty.*

This is a major operative procedure and the operation takes from 2 to 3 hours to perform.

These operations are performed on cases of active chronic suppurative otitis media on infected and vascular temporal bones. The operation consists essentially of an extensive radical mastoid operation with operative toilet of the tympanic cavity and removal of all diseased tissue and toilet of the round and oval windows. Following this toilet the tympanum is reconstructed by a plastic operation in such a way that hearing is restored.

The operation is carried out under a magnification of 10–25 diameters and haemostasis is absolutely essential for success.

FACTORS ESSENTIAL FOR OPERATIVE SUCCESS

The first essential is that the anaesthetic technique must be safe, as these operations may take up to 3 hours to perform. No inflammatory agents can be used, as electrical apparatus is in constant use.

For these operations it is essential that there should be as little bleeding as possible, as haemorrhage or oozing may materially impair, or even ruin, the success of the procedure.

The anaesthetic technique, therefore, should avoid prolonged respiratory depression or apnoea and there must be little or no rebreathing as these factors tend to cause retention of carbon dioxide which results in oozing.

During the operation there should be no coughing or straining upon the endotracheal tube as this leads to increased pressure in the veins of the neck with resulting bleeding at the operation site; for the same reason hyperextension of the neck should be avoided.

The anaesthetic should give rise to a quiet

recovery and avoid postoperative vomiting and straining which again may impair success.

TECHNIQUES

Earlier techniques.

Initially the anaesthetic used was thiopentone, gallamine triethiodide, nitrous oxide-oxygen, minimal trichloroethylene and the use of a hypotensive drug, but this did not prove satisfactory.

The use of the "lytic cocktail" was then tried and proved much more efficient.

Following premedication with papaveretum and scopolamine or morphia and atropine the "lytic cocktail" was given intravenously about 30 minutes before operation. This mixture at first was composed of pethidine 100 mg, chlorpromazine 50 mg, and promethazine 50 mg diluted into 20 ml with sterile water or saline. An endotracheal tube was introduced after injection of 2.5 per cent thiopentone and gallamine triethiodide, and anaesthesia was maintained with nitrous oxide-oxygen and minimal trichloroethylene.

This did not always give satisfactory results as oozing occurred and efforts were made to overcome this by the use of hypotensive drugs, by further doses of chlorpromazine and by use of the head-up position. As a result of these trials the promethazine was omitted, the amount of chlorpromazine increased to 100 mg and Pethilorfan (100 mg pethidine with 1.25 mg levallorphan) substituted for pethidine. Adrenoxyl was also tried pre-operatively but did not appear to be as effective as was hoped.

Present technique.

Children are premedicated with papaveretum 2 mg (1/30 grain) and scopolamine 0.004 mg (1/1500 grain) per stone (6.3 kg) body weight. Adults receive papaveretum 20 mg and scopolamine 0.4 mg (1/150 grain) up to the age of 60 years. Above this age the premedication used is morphia 10 mg ($\frac{1}{6}$ grain) and atropine 0.65 mg (1/100 grain). The premedication is given 1 hour prior to operation and at the same time the patient is given an Anaesthocaine lozenge to suck.

The "cocktail", which consists of Pethilorfan 100 mg and chlorpromazine 100 mg in 20 ml sterile water or saline, is given slowly by intravenous injection 30 minutes pre-operatively, watching carefully for undue respiratory depression or hypotension. The tachycardia which occurs is usually transient. For this technique to have the best chance of success ample time should be given for these drugs to have their effect.

When the patient is sufficiently asleep (a good guide being lack of response to pressure on the supra-orbital nerve), topical spraying of the cords is performed, followed by insulation using the largest tube which, well lubricated with an anaesthetic paste, will pass easily through the cords. If there is insufficient relaxation of the jaws this procedure may have to be aided by the addition of nitrous oxide-oxygen and trichloroethylene, or by $2\frac{1}{2}$ per cent thiopentone and gallamine triethiodide given as necessary.

Maintenance is with nitrous oxide-oxygen (in the proportions 6:2, with a total flow of 8 litres per minute, which helps thereby to prevent retention of carbon dioxide), and with minimal trichloroethylene, if this is necessary. The expiratory valve is kept fully open to avoid the slightest resistance.

With this technique the blood pressure is orthostatic and with about 20° anti-Trendelenburg the blood pressure drops to about 100 mm Hg. Especial care is needed in the case of elderly and hypertensive patients. Slight flexion of the neck also helps to avoid bleeding.

Just before the application of the graft the surgeon applies ribbon gauze soaked in 1:1000 adrenaline to the area.

Should bleeding prove to be troublesome despite these measures a hypotensive drug is used, but with this technique this has seldom been necessary.

POSTOPERATIVE COURSE

There have been no postoperative complications and no restlessness or vomiting which might impair the success of the operation.

The safety and success of this technique, which has been used in patients whose ages range from 5 to 58 years, encouraged its continuation and it was felt that this description might prove helpful to those contemplating these operations.

SUMMARY

The operations of myringoplasty and tympanoplasty are briefly described.

An account is given of the factors essential for a successful outcome and of the evolution of the present technique.

A safe and satisfactory anaesthetic technique using Pethilorfan and chlorpromazine is described for these operations.

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ON CHLOROFORM AND OTHER ANÆSTHETICS

THEIR ACTION AND ADMINISTRATION

BY

JOHN SNOW, M.D.

Licentiate of the Royal College of Physicians

(*Continued from page* 346)

A patient, attended in her confinement by Mr. Colambell of Lambeth, in 1853, to whom I gave chloroform, had been long under the care of Dr. Williams with cavities in the lungs. I heard very lately that she was still living.

A patient of Mr. Robert Dunn, to whom I gave chloroform in her confinement, was at the time in a state of insanity.

In one of the patients whom I have attended with Dr. Arthur Farre, there was separation of the recti muscles of the abdomen; which there is no doubt must have taken place gradually during pregnancy. The patient was but twenty years of age, and in her first labour. Quite early in the labour, before the pains were at all strong, Dr. Farre and I observed that the abdomen was of a peculiar form, the uterus projecting very much forwards, whilst there was slackness in the flanks. The abdominal muscles did not assist the pains at all and it was probably from this cause that the labour progressed slowly and was terminated at last with the forceps. The recti muscles recovered their position by careful bandaging.

The chloroform has always been left off as soon as the child was born, but a little has been administered again on several occasions during the expulsion of the placenta. The placenta has generally been expelled very soon in the labours in which I have given chloroform usually in about five minutes. There has hardly ever been uterine hæmorrhage of any amount, except in patients who had suffered from it in previous labours. In a case attended by Mr. Nathaniel Ward, however, there was a slight hæmorrhage before the birth of the child, and about an hour afterwards there was a considerable hæmorrhage which made the patient feel rather faint for some hours. She afterwards went on favourably, however. She was a young woman who had had several children.

A patient, to whom I was recommended by Sir John Forbes, inhaled chloroform in three confinements. She recovered favourably from the two first; but on the third occasion, after going on favourably till the fifth day, she was attacked with puerperal fever, and died on the seventh day from her confinement.

I am not aware that more than one death has been recorded as having occurred from chloroform during labour; and this took place in England, in 1855, when no medical man was present.* The patient had inhaled chloroform in America in a previous labour; but her medical man, on the last occasion, who was her particular friend, forbad that agent, and said that if she was determined to have it, he would not attend her. She procured chloroform

* See Medical Times and Gaz., 1855, vol. i, p. 361.

unknown to him, and a number of scents to put on her handkerchief and hide the odour of it from him. He went to bed in the house, and was not called up till his patient had been dead about an hour. The monthly nurse, who had procured the chloroform for the patient, said that she snored very loudly for an hour after she fell asleep. About five drachms of chloroform were used from the bottle, and the handkerchief from which it was inhaled remained close to the patient's face till she died. The death seemed to have taken place very slowly, and the monthly nurse was extremely stupid to allow the patient to die. It may also be remarked that the accident would not have taken place except for the medical man's extreme objection to the use of chloroform.

The chloroform has been occasionally blamed by the friends of patients, or medical men opposed to its use, in cases where patients have died from puerperal convulsions or other causes, so long after the vapour had been left off that it could not be the cause of death. The following case shows how easy it would be to make a mistake with respect to the effects of chloroform. Soon after its introduction, I was requested to administer it to the wife of a medical man who had a great desire for it in her confinement. Mr. Propert was to attend the lady. I was sent for late one evening, but as there were no pains at the time when I arrived, I was requested to go to bed in the house. After a time, I was called by a servant, who told me that the baby was born, and that Mr. Propert was sent for. I found that the birth had been so sudden that the husband, who was in the room, could not get to the bed side before the child was born. Mr. Propert arrived, and I went home, leaving the patient very well. Mr. Propert informed me, that after I left the patient went into such a state of syncope as to make him think she was going to die, and continued so for some time. She ultimately recovered. There was no hæmorrhage or any other cause to account for the faintness, and I understood Mr. Propert to say, that if the patient had inhaled chloroform, he should have blamed it for the condition into which she lapsed.

THE INHALATION OF CHLOROFORM IN MEDICAL CASES

Neuralgia. When the pain of neuralgia is not extremely severe, it may be removed by the inhalation of chloroform without causing unconsciousness; but when it is very severe, it is necessary to make the patient unconscious before the pain is suspended. In some cases of neuralgia of the face, the pain is so severe that the signs of it remain after the patient is rendered unconscious, and only disappear when he is quite insensible; and then, as the insensibility passes off, the hand is raised to the face, and the contortions of the features return before the patient awakes to be aware of his suffering. When the mental branch of the fifth nerve is affected, the paroxysms of pain are accompanied by a motion and smacking of the lips. In a hospital patient I have seen this when he was awake, but in a gentleman only when his consciousness was removed by the chloroform, and before complete insensibility was induced; when awake, he restrained the impulse to this kind of motion of the lips.

In administering chloroform it is desirable to continue it steadily and gradually

till the pain is relieved; and if the patient is rendered unconscious before the pain is removed, to continue it till all signs of suffering disappear. After the first inhalation of the vapour, the pain will generally return in a few minutes, but when again subdued, it will not return so quickly; and after it has been suspended a few times by the repetition of the chloroform during the space of an hour or so, the pain is usually removed either permanently or for two or three hours. In some cases I have had to repeat the chloroform occasionally throughout the day, and, on one or two occasions, for two or three days in succession. The chloroform can, in general, only be considered a temporary remedy, and therefore such other medicines should be applied as may be thought advisable.

When I have prescribed chloroform in a liniment, to be applied to the face, the patient has often found out that he obtained more relief by smelling at the liniment than by applying it. Chloroform generally gives great relief, however, when applied locally in neuralgia, either alone or mixed with camphorated spirit; it is advisable to apply it on a piece of lint or blotting paper, which should be covered over with tinfoil, or some other impermeable substance, to prevent the evaporation. It causes about as much heat and uneasiness as a mustard poultice, before it relieves the pain.

Spasmodic Asthma. On November 12th, 1850, I administered chloroform in the Hospital for Consumption, at Brompton, to a married woman, aged thirty-five, a patient of Dr. Cursham. She was in a fit of spasmodic asthma, but was the subject also of chronic bronchitis. Twenty minims of chloroform were inhaled from an inhaler. It gave immediate relief, producing a momentary state of unconsciousness, or a state bordering on it. In a few minutes the difficulty of breathing gradually returned, but not to the same extent, and the inhalation was repeated with a like effect. The difficulty of breathing returned less quickly and severely; and after a third inhalation of twenty minims she was completely relieved, and could lie down. The patient had a good night, and was better next day. On the 14th, she had another fit of spasmodic asthma, which was relieved completely by the chloroform in the same manner as the previous one. This patient inhaled extract of stramonium every evening, by a method which will be described further on.

Other cases of spasmodic asthma have been relieved as readily and completely; but in one or two cases, in which the difficulty of breathing seemed to depend on disease of the heart, the relief was not so great; the patient went to sleep, but the breathing remained embarrassed.

Spasmodic Croup. I have administered chloroform in seven cases of this complaint. It was recommended in every instance by Dr. Fergusson, and in all the cases ended in recovery. The children were from eight months to two years of age; the majority being about a year. I always gave enough chloroform to cause a state of unconsciousness, for which a few minims suffices in a young child, and when the effect passed off, or nearly so, I repeated the dose. I generally gave five or six doses in the course of about half an hour, after which the child would often sleep for two or three hours. In the milder cases it was repeated once a day; but in

the more severe cases it was continued, in the above manner, twice a day. I administered it to a patient of Dr. Van Oven, respecting whom Dr. Fergusson had been consulted, for fifteen days, twice every day, excepting the last three days. This child was very ill when the treatment was first commenced, having a severe fit of spasmodic breathing every five minutes. When the chloroform is given during the spasm, it is desirable to give it very cautiously.

Mr. W. J. H. Cox read a paper on the treatment of laryngismus stridulus, with chloroform, at the London Medical Society, in 1850. He had entrusted the administration of it to the mother or nurse, and directed it to be given whenever the spasmodic breathing should come on. I am inclined to think that this would be the best way of giving it, if one could be quite sure of the intelligence of the party to whom it was entrusted.

Hooping Cough. I have only administered chloroform in two cases of this complaint. It was recommended in both cases by Dr. Fergusson. One of the children was extremely ill of bronchitis, and it died. The other child recovered, but the chloroform was not continued. I am not aware that chloroform has had any fair trial in hooping-cough. It should be given whenever a fit of coughing comes on.

Infantile Convulsions. I have administered chloroform in two cases of this disease, with the effect of relieving the convulsions, but the children died. They were both extremely ill before the chloroform was administered. One was the patient of Mr. Walter Bryant, and Dr. Seth Thompson was consulted about it. A case has been related by Dr. Simpson of Edinburgh, in which the chloroform was continued for a day or two, and in which the infant recovered.

*Delirium cum Tremore.** Some cases have been related in the medical journals, in which this complaint was treated successfully by chloroform alone; but I prefer to use this agent only as an adjunct to the treatment by opium. Sometimes the patient is so violent and suspicious that he cannot be made to take opium; but it is much easier to make a person breathe a medicine, than swallow one. It is only necessary to hold a patient, and to apply the chloroform near his face, and he is obliged to breathe it, and as the effect of it subsides he recovers the power of swallowing before his delirium returns; for whilst he is still unconscious, he will swallow whatever is poured into his throat. Opium can be administered, and the chloroform can be repeated occasionally so as to keep him asleep for an hour or two till the opium takes effect and prolongs the sleep. It is a great advantage of chloroform that the delirium may be subdued in a few minutes by it, and can be kept away till opium takes effect.

In certain cases of delirium cum tremore, such a quantity of opium is taken without procuring sleep, that the medical attendant has, what I believe to be, a well-

* Dr. Watson defends the original name of this complaint, delirium tremens. He says:—"But they who object to *delirium tremens* appear to see no harm in delirium ferox: whereas it is just as incorrect to say *delirium* is fierce, as to say that it trembles: it is the patient who is furious, even as it is the patient who trembles." Now, in speaking of a patient, we may speak either of his mind or his body: we may say that a person is learned, or that he is fat. A patient may be fierce on account of the kind of delirium with which his mind is affected, and the term ferox applies both to him and the complaint; but the act of trembling affects only his body.

grounded fear of giving more. A patient whom I saw with Mr. Peter Marshall, in April 1850, had taken ten fluid drachms of laudanum and two grains of acetate of morphia, within twenty-four hours of my seeing him, without any sleep being procured. He was put to sleep immediately by chloroform which was repeated on the following day. The patient got quite well in a few days.

In December 1851, I saw a patient who had had no sleep for four days, except three intervals of a quarter of an hour each, although a great deal of opium had been given. He was very violent; and for the last twelve hours had spat out all the medicine that was given to him; his pulse was small and very rapid. He was made insensible in a few minutes, and the chloroform was repeated, at intervals, for half an hour, so as to keep him unconscious. Fifty minims of tincture of opium were given in one of the intervals. I waited an hour and a quarter after the chloroform was discontinued; the patient was still sleeping, and his pulse was less frequent. I learnt that when he awoke he was quite free from delirium, and he was well in a few days.

Delirium in Fever. In November 1857, I administered chloroform to a youth of seventeen, who had been ill of typhoid fever for sixteen days. He had been in a state of constant delirium for upwards of forty-eight hours without having the least sleep, although he had had tincture of opium in divided doses to the extent of forty-five minims, and had taken a tablespoonful of wine every four hours. The chloroform was continued gently for half an hour; he slept for an hour afterwards, and at intervals during the night. He was a little better in the morning; and the delirium was not again so violent as it had been. He died on the nineteenth day of the fever, from a recurrence of diarrhoea.

Dr. Fairbrother, of Bristol, gave small doses of chloroform by inhalation, with the best effects, in a case of typhus fever, in the Bristol Infirmary. The patient was delirious and worn out for want of sleep, her life being in fact despaired of. She inhaled the chloroform occasionally for several days, sleep being always procured when it was applied, and she recovered without any other medicine.*

Hydrocephalus. I administered chloroform on two occasions, for half an hour at a time, to a child, seven years old, when delirious and screaming violently, in this complaint. The child was much relieved by the inhalation, but it died on the fourteenth day of the disease.

Tetanus. I have notes of three cases of tetanus in which I have administered chloroform. The first was a patient of the late Mr. Keate, in St. George's Hospital, in February 1849. It was a girl, fourteen years old, who had received some severe burns in the face and various parts of the body, a fortnight previously. Four days before inhaling the chloroform, she was attacked with symptoms resembling those of chorea, but for the last two days the complaint was recognised to be tetanus. There was rigidity of the spine and jaws, and of one arm, which was flexed. Spasms came on every minute or two, affecting, more particularly, the head and the arm. I commenced to give chloroform very gently at four in the afternoon. It prevented the spasm before consciousness was quite

* Med. Gaz., vol. xli, 1848, p. 102.

removed. Whenever the spasm offered to return, the inhalation was repeated with the effect of stopping it. The chloroform was continued till half-past five, with the effect of keeping the spasm away; and the patient took some drink during this time, better than she had done previously. I saw the child again at eight o'clock in the evening, and found that the spasms had returned soon after I had left, and had continued as before. The chloroform was given again at intervals for an hour and a half, with the effect of keeping away the spasms, and inducing sleep; but I found that the child was getting weaker, and would die even if the spasm was entirely prevented. She died at a quarter past eight the following morning. There was no inspection of the body.

The next case was a patient of Mr. Propert, a boy, ten years of age, who had suffered from sloughing of the skin of the inferior extremitites. The tetanus came on during the healing process, whilst the greater part of both extremities was in a state of ulceration, and covered with healthy granulations. The patient was in a very irritable and feeble state, and his pulse was 150 in the minute. He was made insensible, and the chloroform was repeated twice in the space of half an hour. No relaxation of the muscles of the jaws was produced, although the effect of the chloroform was carried as far as seemed safe in such a subject. He died twelve hours afterwards.

I administered chloroform lately to a patient of Mr. Salmon in St. Mark's Hospital. He underwent an operation by ligature for prolapsus ani and hæmorrhoids on March 1st; on March 5th tetanus commenced, and on March 7th chloroform was administered whilst Mr. Salmon removed some sloughs from the anus; and it was repeated occasionally afterwards. The patient was a man, fifty-two years of age; he was the subject of kidney disease, and the tetanus was extremely severe. He had had four doses, each containing a fluid drachm of laudanum, between the time when the tetanus commenced and his inhaling the chloroform. His pupils were contracted, and he was made insensible by an extremely small quantity of chloroform. He was, in fact, very much under the influence of opium, although the spasm of the tetanus prevented his sleeping.

Chloroform affords great relief to the patient affected with tetanus, and it probably increases the prospect of recovery in cases which are not too severe and acute.

Epilepsy. Dr. Todd at one time had chloroform administered by inhalation, in King's College Hospital, to the extent of causing insensibility, at stated intervals, in cases of epilepsy, and he thought with advantage. I have frequently administered chloroform for surgical operations to patients who were subject to epilepsy, and have very rarely found it produce any approach to a fit.

In July 1850, I administered chloroform to a boy, seven years old, in an epileptic fit, which had lasted about an hour when the inhalation was commenced. He had had fits previously, the last of which had occurred a year before, but none of them had lasted so long as the existing one. He had eaten nine new potatoes for his dinner, at one o'clock, and the fit came on about eight. I found the abdomen swollen and very tympanitic. There was constant convulsive motion of the right arm, and of

the neck; the latter drawing the head to the right side. The mouth was also drawn to the right at each convulsive motion. The chloroform was given by putting a few minims at a time on a handkerchief, and holding it to the mouth and nostrils. It caused immediate cessation of the convulsions every time it was applied. The convulsions, however, returned again in a minute or two. In the intervals that he was partially under the influence of the vapour, he breathed easily without stertor. The convulsions became gradually less severe, and ceased entirely ten or fifteen minutes after the commencement of the inhalation.

Puerperal Convulsions. I have not been called to any case of this complaint since chloroform has been in use; but some cases have been related in the medical journals in which the inhalation of chloroform has been employed with a favourable result. One case is related by Mr. Henry Rudge, of Leominster.* When the chloroform was administered, the patient was in violent convulsions which came on in frequently succeeding fits. The os uteri was dilated, and the head presenting. The pains were entirely arrested. The chloroform was administered by twenty minims, at intervals, on a folded handkerchief. The convulsions, after a few inhalations, entirely ceased, and Mr. Rudge extracted the child without difficulty. There was another child with the head presenting: it was delivered with the forceps. The placenta was delivered with the hand on account of smart hæmorrhage. There was only one attack of convulsions after delivery, and the patient recovered favourably. It was her first labour, and her age was twenty-three years.

A case of puerperal convulsions was related by Mr. Andrew Bolton to the Newcastle and Gateshead Pathological Society.† His patient, aged twenty-two, was at the full period of her first pregnancy. The os uteri was high, slightly dilated, and extremely rigid. She was treated at first by bloodletting, and full doses of morphia. Mr. Bolton says: "As her condition appeared hopeless should the paroxysms continue, chloroform was administered on a piece of linen, in half-drachm doses, and its full effects kept up for three hours. At two P.M., there was a slight return of convulsion; skin warm and perspiring; the os uteri was found steadily dilating; and from her uneasy movements, it was apparent that uterine action had begun.

"Half-past three. The membranes were ruptured; and brisk uterine action ensuing, a dead child was expelled, immediately followed by the placenta. She regained her senses during the expulsive efforts, but appeared entirely ignorant of her previous condition. Recovery followed without any bad symptom.

"In conclusion, I would remark, that the convulsions were in no measure mitigated by the depletion, which was carried to the utmost; nor was there any yielding of the os uteri until chloroform was inhaled."

The urine was not examined in either of the above cases, and it is not stated that œdema was present.

Hysterical Paralysis and Contractions. In December 1851, I administered chloro-

* Association Med. Journ., 1853, p. 706.

† See Med. Times and Gaz., 1853, vol. ii, p. 412.

form in Charing Cross Hospital to a young woman about twenty-five, a patient of Dr. Chowne. She kept her left knee in a semi-flexed position, and would not allow it to be moved. She had been in bed in the hospital for two months. She inhaled the chloroform reluctantly, and, after becoming unconscicous, she breathed and sobbed in a hysterical manner. When insensible, the limb went down flat on the bed, the knee being quite movable. A straight splint was applied, and the limb was secured to it with bandages. I was informed that in a few days she contrived to get her leg bent again. She was the domestic servant of a nobleman. It was evident that there was nothing the matter with her limb, and that it was only influenced by her volition, which was perverted by the hysteria under which she was labouring.

In November, in the same year, I administered chloroform in the same hospital to another patient of Dr. Chowne, whose case was more obscure and complicated. The patient was a woman, aged thirty-three, who represented that for several months she had been unable to open her mouth, or to speak, and that she had, for the same length of time, been paralyzed in the left arm and leg. The affection, it was said, came on suddenly, in a kind of fit, which was followed by unconsciousness for three or four weeks. It was also said, that she had one or two fits the previous year, after which she was unconscious for a long time. The patient was quite conscious before inhaling the chloroform, and replied to questions by nodding or shaking the head, or by writing on a slate. She was unmarried, and had not menstruated for some months past. The chloroform was administered with a view to ascertain whether or not she was feigning. On first becoming unconscious, the patient breathed in a sobbing and hysterical manner. The chloroform was given very gradually; and as she became more affected, there were some struggling and rigidity, when the right arm and leg were moved about a good deal. The left arm and leg were also distinctly moved, but not above a tenth part as much as the extremities of the opposite side. When the patient was quite insensible, the limbs being relaxed, the pupils turned upwards, and the conjunctiva insensible, attention was turned to the jaws, which were still firmly closed, but they were opened by using a moderate degree of force with the fingers. The effect of the chloroform having been allowed in a great measure to subside, it was again administered, when the movements of the limbs recurred, and there was the same difference between the motion of the right side and that of the left, as before. When I left the patient, more than half an hour after the chloroform was discontinued, she had not opened her eyes or answered questions; and she did not do either for six days. I saw her five days after the chloroform. The pulse was very rapid on my first going to the bedside, but its frequency subsided in a few minutes. On my raising the eyelid, she turned her eye about, as if endeavouring to hide the pupil under the lid. On the following day, she answered questions by nodding and writing on a slate, and was, in other respects, the same as before inhaling the chloroform.

The great difference in the amount of motion in the limbs of this patient, under the influence of chloroform, showed that

the paralysis of the left side was not a mere pretence. It is, indeed, possible that the absence of motion in the limbs of the left side, for several months, would cause them to move less than the opposite ones during the action of chloroform; but it is not to be supposed that the patient would keep these limbs in one posture during the night, and when no one was present, without ever moving them, unless she herself believed that they were paralyzed. I looked on the woman as a sick person, and not a mere impostor; for although she appeared to exaggerate her symptoms, and to have a good deal of pretence and affectation, this circumstance arose, no doubt, from her complaint.

In April 1853, I administered chloroform four times to a patient of Dr. Arthur Farre, a girl of fifteen years of age, who was affected with a contraction of the flexor muscles of the left thigh and leg, of the muscles which bend the body to the left side, and those which bend and turn the head to the same side, in consequence of which the leg was drawn up, and the body and head were curved greatly to the left side. The contraction of the muscles had lasted for several weeks, but she had been ill for a much longer period, her illness having commenced with a fever. She took an extremely small quantity of nourishment, and was very thin. Her bowels were moved with difficulty. The pulse was very feeble and small, and there was a tendency to coldness of the surface. An eminent surgeon in the provinces had expressed his opinion that the distortion of the limbs and trunk was a feigned disorder; but the action of the chloroform proved that he was altogether in error. The muscles became completely relaxed when the patient was quite insensible, and the limbs and trunk and head could be readily moved into any position; but as the effects of the chloroform subsided, the deformity returned on each occasion before the patient recovered her consciousness. Neither the chloroform nor any other measures were of any service, and Dr. Farre informed me that the patient died a few weeks after I saw her.

Mania. I have been informed of several cases in which chloroform has been administered in acute mania, with the effect of calming the patient and procuring sleep. I have administered it in two cases with the same temporary advantage. In one of the cases, the patient was persuaded to inhale it; in the other he had to be held by three keepers till he was unconscious. An eminent and well-known scientific man, who became insane some years ago, refused to take food. It was found that after being made unconscious by chloroform, he would take a meal just as he recovered from its effects, and the chloroform was given before every meal for a long time.

Spasmodic Pain. In August 1851, I administered chloroform to a woman who was labouring under a severe paroxysm of spasmodic pain in the abdomen. The pain was completely removed, without altogether causing unconsciousness. An opiate was given to prevent the pain from returning.

I have not had the opportunity of administering chloroform during the passage of calculi down the ureters, or of gallstones; but there can be no doubt that it would be of the greatest service in such cases. If Dr. Griffin had been provided with chloroform when he attended the late

Mr. Augustus Stafford with an attack of gall-stones,* he would have been able to relieve his patient in five minutes, instead of taking two or three hours to produce relief by opium. There would have been no occasion for the venesection, which was carried to thirty ounces. And at the end of the attack, on Dr. Griffin leaving his patient for the night, if chloroform had been employed, he would have left him without any appreciable amount of narcotic in his system. As it was, however, he left him with a quantity of opium unabsorbed from the alimentary canal. The bandage got displaced from the arm; there was an additional hæmorrhage, the opium became absorbed more quickly, and a dangerous state of narcotism was induced.

Frequent and long-continued Use of Chloroform. Many patients have inhaled this agent hundreds of times, and it continued to produce insensibility as readily as at first. The dose does not require to be increased on account of its long use. I was informed of the case of a lady who was affected with a painful cancer, and was attended by the late Mr. Keate and Mr. Henry Charles Johnson. She inhaled chloroform at frequent intervals, by day and night for a very long time, consuming three or four ounces in the twenty-four hours.

In November 1851, a surgeon in the north of England wrote to me respecting one of his patients, a lady, who had inhaled a great deal of chloroform, on account of neuralgia of the uterus. He said that, during that year, and principally within the last six months, she had inhaled at least two hundred ounces; that she often inhaled as much as three ounces in a day; and that it seemed to have produced very little effect on her general health, except that she seemed to be more susceptible of pain. He said that he had reluctantly yielded to the entreaties of his patient to administer it so often, and he wished for my opinion respecting the propriety of continuing its use, and what effect it would be likely to produce.

I advised that the chloroform should be continued as long as the severity of the pain rendered it necessary; and expressed my opinion, that it would produce as little ultimate effect as any other narcotic which might be used to relieve the pain. I saw the surgeon in September of the following year. He informed me that the chloroform was continued for some time after he had written to me; but that his patient had recovered from her complaint, and had left off the chloroform, and was in good health.

Mr. Garner, of Stoke-upon-Trent, has related the case of a lady, affected with neuralgia, who inhaled sixty-two ounces of chloroform from her handkerchief, in twelve days.†

* Med. Times and Gaz., 1857, vol. ii, p. 553, and 600.

† Med. Times and Gaz., 1856, vol. ii, p. 528.

CORRESPONDENCE

LEVALLORPHAN IN ANAESTHESIA

Sir,—While there can now be little disagreement with the conclusions reached by Hunter (1958), his method of measurement of the minute volume calls for comment.

Finding that a high fresh gas flow rate caused an error in the measured minute volume, he reduced the flow to basal requirements during the period of measurement. Using the Coxeter-Mushin circuit which he illustrates (with the addition of a relief valve on the patient's side of the expiratory valve) we have measured the inspired and end-tidal CO_2 concentration using an infrared analyzer. A model patient was used with a tidal volume of 380 ml (ATPS), respiratory frequency of 16 b.p.m. and CO_2 output adjusted to give an expired CO_2 "plateau" value of approximately 5 per cent. Fresh soda lime was used for the experiment which lasted less than 40 minutes. Measurements were made when the fresh gas flow rate was reduced from 8 l./min to basal flow and also to 2 and 4 l./min (fig. 1).

Reduction of the fresh gas flow rate caused a remarkably rapid increase in the inspired CO_2 concentration. With a conscious subject the inspired CO_2 concentration rose rapidly but hyperventilation prevented the rise in the end-tidal concentration. While we have no data of the effects of the inhalation of 3 per cent CO_2, which presumably occurred during the measurement of the minute volume, figure 2 shows the respiratory response to the inhalation of 4 per cent CO_2 in the anaesthetized patient.

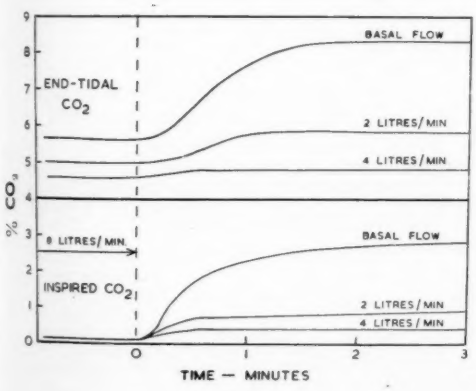

FIG. 1

Changes in the inspired and end-tidal CO_2 concentration resulting from the reduction of the fresh gas flow with the Coxeter-Mushin gas circuit.

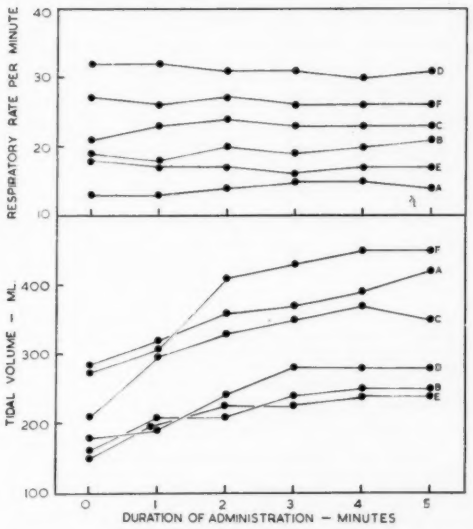

FIG. 2

The respiratory response to the inhalation of 4 per cent CO_2 by six anaesthetized subjects (A—F).

It is a fundamental principle of measurement that the method should not influence the quantity being measured. While it is possible to conform to this requirement when measuring the minute volume with a gas meter during anaesthesia (Zinberg and Jensen, 1954) such a method cannot compare in accuracy with spirometry. With any of the anaesthetic gas circuits in common use the minute volume may be measured by continuous

flow spirometry, the accuracy of which is unimpaired by the fresh gas flow rate (Nunn, 1956).

RONALD WOOLMER
J. F. NUNN
Research Department of Anaesthetics, Royal College of Surgeons of England

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Zinberg, S., and Jensen, N. K. (1954). A method for measuring tidal and minute volumes in patients under regional and general anaesthesia. *J. thorac. Surg.*, **28**, 85.

Sir,—I am most interested in the observation of Dr. Woolmer and Dr. Nunn that carbon dioxide builds up so rapidly with the Coxeter-Mushin absorber. Mushin (1942) investigated this point in the original apparatus and found no such tendency, though he quotes some work of Frankis Evans (1938) in which the latter found a rise in carbon dioxide content of inspired gas to about 4 per cent with a comparable machine. Mushin's work was done with the Mark I apparatus. I have been unable to trace any reference to studies of later versions of the machine, though Cullen (1955) using an infrared analyzer (Cullen et al., 1956) found a higher minimum amount of carbon dioxide in the inspired gas than in that of true circle absorbers. I used a Mark I apparatus in my studies and would be most interested to learn what type Dr. Woolmer and Dr. Nunn investigated. In view of their letter, however, I have reconsidered this aspect of the basis of my work.

Among the 36 patients whose respiratory displacement I have studied by this method there were a number in whom measurements were carried out in circumstances in which a hyperpnoea in response to accumulating carbon dioxide might have been expected to occur. In two such cases the absorber was deliberately cut out in order to measure the ensuing hyperpnoea. In others measurement of ventilation was continued for a period of 2 to 4 minutes in order to obtain a base line to which to relate the change in respiratory displacement produced by some drug to be given subsequently. The resulting change in respiratory minute volume are shown in tables I and II. It will be seen that the variation in the group measured for control purposes is very much smaller than those where a respiratory centre responded to accumulating endogenous carbon dioxide and that for the first 3 minutes of measurement at least the error is well within the overall variation of 10 per cent. For these reasons I feel that my results are in fact even more significant than the findings of Dr. Woolmer and Dr.

TABLE I
The response to endogenous carbon dioxide allowed to build up in a Coxeter-Mushin closed circuit (Mark I).

	Respiratory displacement		
	Case 23 (l./min)	Case 8 (l./min)	Mean as percentage of initial displacement
Before cutting absorber out ...	4.2	5.7	100
First minute after	5.6	5.7	117
Second minute after	6.8	6.0	132
Third minute after	6.4	6.6	134
Fourth minute after	7.4	7.4	150

TABLE II
The variation in respiratory minute volume during continuous measurement utilizing a gas meter in the expiratory hose of a Coxeter-Mushin (Mark I) anaesthetic apparatus.

	Number of observations	Mean respiratory minute volume as percentage of that in the first minute
First minute	20	100
Second minute	20	102
Third minute	17	106
Fourth minute	8	118

Nunn would suggest, though I freely admit that, had the latter's apparatus been available to me when I began these studies in 1954, I should have used it in preference to my own.

A. R. HUNTER
The Royal Infirmary, Manchester

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Sir,—Dr. Hunter has kindly sent us a copy of his reply to our letter. We used the Coxeter-Mushin Mark I and I wondered if a footnote to that effect might be appropriate.

J. F. NUNN
Research Department of Anaesthetics, Royal College of Surgeons of England

RESPIRATORY MEASUREMENTS IN THE THEATRE

Sir,—In the Editorial of your June issue, you mention that it would be an advantage for the anaesthetist to be able to measure tidal volumes in the theatre.

The combination of the accurate meters which we enjoy, and the many varieties of non-rebreathing valves available, enables the anaesthetist to assess and indeed control the tidal and minute volumes with reasonable accuracy.

This method has the added advantage of being the most efficient way of giving nitrous oxide, the need for supplements being lessened to a marked degree.

F. G. ETHERIDGE
Chertsey, Surrey

DR. MAGILL'S 70TH BIRTHDAY CELEBRATION

We have great pleasure in reporting a most pleasant occasion. Dr. and Mrs. I. W. Magill were entertained to dinner by their friends in the Council Room of the Royal College of Surgeons on July 23, 1958, to celebrate Dr. Magill's 70th birthday. Those present were: The Dean of the Faculty of Anaesthetists (Dr. Geoffrey Organe), Drs. S. M. Anderson, H. K. Ashworth, A. J. W. Beard, R. J. B. Broad, A. S. Daly, G. Edwards, F. T. Evans. H. W. Featherstone, A. H. Galley, T. Cecil Gray, J. Gillies, V. A. Goldman, V. F. Hall, R. Jarman, B. R. M. Johnson, K. G. Lloyd-Williams, W. A. Low, W. S. McConnell, R. Machray, A. D. Marston, Professor W. W. Mushin, Drs. B. L. S. Murtagh, M. D. Nosworthy, Professor E. A. Pask, Drs. E. S. Rowbotham, R. F. Woolmer and J. B. Wyman.

The toast of the evening, "Dr. and Mrs. Magill", was proposed by Dr. Machray. It was followed by expressions of good wishes and gratitude on behalf of the Association of Anaesthetists by the President (Dr. T. Cecil Gray) and by many impromptu speeches and tributes by those whom Dr. Magill had anaesthetized, those who had anaesthetized him, those who had been taught by him, those who had deputized for him and those from "North of the Border". A special tribute was made by Dr. E. A. Rowbotham who was Dr. Magill's early colleague in the pioneering work on endotracheal intubation.

FACULTY NEWS

ELECTION OF DEAN AND VICE-DEAN

At the Meeting of the Board of the Faculty of Anaesthetists in the Royal College of Surgeons on June 25, Dr. Geoffrey Organe was elected Dean and Professor E. A. Pask, O.B.E., was elected Vice-Dean of the Faculty for the coming year.

HONORARY FELLOWSHIPS

On the recommendation of the Board of Faculty, the Council of the College has elected the following to the Honorary Fellowship in the Faculty: Dr. I. W. Magill, C.V.O., Dr. R. J. Minnitt, Dr. E. S. Rowbotham, Sir Henry Souttar, and Dr. R. M. Waters. We extend to these distinguished gentlemen our most sincere congratulations.

Extracorporeal Circulation. Compiled and Edited by J. Garrott Allen, assisted by F. D. Moore, A. G. Morrow and Henry Swan II. Published by Charles C. Thomas, Springfield, U.S.A. Pp. 518; illustrated. Price 57*s.* 6*d.*

This book is the finest example of "symposium reporting" that has ever come our way. It is a splendid tribute to the industry and efficiency of the editors, publishers and authors. The story is as follows: In the early Spring of 1957 (according to the Preface), the National Advisory Heart Council, which is apparently the chief policy-making group of the National Heart Institute, suggested that a conference be held to discuss developments in the field of extracorporeal circulation, and the Surgery Study Section was asked to arrange this get-together. A group, large enough to cover the many individuals who had made contributions in this field and yet small enough to discuss the problems efficiently, was assembled in the second half of September 1957. This book contains the many papers given on this subject at that meeting and the discussions with which they were followed. There are contributions from the great pioneers in this work both on the surgical and physiological aspects, and most up-to-date results are quoted. It is astonishing that the publishers were able to have the book out in such an attractive, well illustrated and exquisitely bound form within the first quarter of this year. Some may regret the absence of an index, but this is hardly to the disadvantage of the reader as the detailed table of contents is extremely helpful.

The first part of the book describes the various pumps and oxygenators that have been produced and lists the ideals which should be achieved. In the second section is a full discussion of the physiology of perfusion, and in the third part detailed technical subjects as "Problems in Coagulation" and "The Effects of Extracorporeal Circulation on the Brain" are discussed. Finally there is a series of papers and discussions on the Metabolism of the Heart, Coronary Blood Flow and Induced Asystole.

It must be obvious that this is a volume of the utmost importance to all workers in this field. Its appearance is a tribute to the great advances which have been made and a healthy augury of those to come.

T. Cecil Gray

A Manual on Cardiac Resuscitation. (2nd edition.) By Robert M. Hosler. Published by Thomas, Illinois. Pp. 208; illustrated. Price 42*s.*

This volume appears at a time when the treatment of cardiac arrest is receiving widespread attention. Surgeons and anaesthetists can no longer feel apprehensive about entering the chest, and this manual rightly encourages no delay in the presence of the appropriate danger signals. Following an exciting review of the aetiology of the condition, the author discusses preventive measures and details the equipment which should be immediately and subsequently available. He is on surer ground in his description of the steps in cardiac resuscitation which are clearly defined, though it would be even better to begin with "what to do" rather than "things not to do". It is pleasant to find the term hypoxia correctly used in contrast to the usually incorrect anoxia, and equally agreeable to find the admission that when an operation can be done in two hours, there are advantages in *not* taking four.

The Report on "Deaths Associated with Anaesthesia" was promoted, however, by the Association of Anaesthetists and not by the English (sic) Ministry of Health. On page 84, a baby's trachea may be only 1 inch (2.5 cm) in length, but happily it is more often 4 cm, even at birth. This book claims to be completely reset from new type but further correction is much needed. There is scarcely a page upon which words are not mutilated by hyphens to produce at all costs the necessary even margin—to encourage intercostal splitting does not demand such realistic typesetting. The appearance of this manual is timely; its presentation is a little dramatic ("Oxygen, The Fuel of Life") in the style of Man versus Death, but the material is sound and the essentials are not overlooked.

H. H. Pinkerton

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